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A Case-Control Study of Occupational and Dietary Factors in Colorectal Cancer in Young Men by Subsite[1]

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ABSTRACT

With the hope that exposures responsible for colorectal cancer might be especially obvious among those in whom it develops early, 147 men with colorectal carcinomas first diagnosed between the ages of 25 and 44 years were compared to neighborhood controls. Physical activity on the job was protective for tumors located in the transverse and descending portions of the colon. Rectal cancer and to a lesser extent sigmoid cancers were associated with jobs in which dusts or fumes were inhaled, especially if those jobs were held for long periods in young adulthood. While risk for rectal cancer did not seem to be limited to any particular type of dust or fume, the excess risk was strongest for wood and metal dusts. Consumption of fruits and vegetables and a preference for whole grain breads were protective for colon but not rectal cancers, while consumption of deep fried foods and barbecued/smoked meats increased risk at specific subsites. Beef intake, alcohol consumption, and cigarette smoking appeared to play little or no role at any subsite.

INTRODUCTION

Like most malignant epithelial tumors, carcinomas of the colon and rectum increase in frequency with increasing age and rarely occur before the fifth decade of life. In Los Angeles County, fewer than 5% of these tumors are diagnosed in persons under 45 years of age. With the hope that environmental or life-style exposures responsible for these diseases might be especially striking among those in whom they develop early in life, we conducted a case-control study in young men.

Environmental factors play a major role in the etiology of colorectal cancers since international differences in incidence are at least 10-fold in magnitude and migrants acquire the levels of their new neighbors within two to three decades after migration (1). The most commonly cited environmental hypotheses are dietary, but case-control studies have produced inconclusive or conflicting results regarding most foods and nutritional factors (2). For many years occupational studies have tentatively linked colorectal cancer to asbestos (3, 4) and to work with metal and textiles (5). More recent investigators have observed excess cancer of the large bowel among woodworkers (6–8) and men with sedentary jobs (9–12). Colorectal cancer in adolescents has also been linked to agricultural herbicide and pesticide exposure in childhood (13, 14).

Colon and rectal cancers are often combined in etiological studies, but the social class gradients for the two sites tend to be in opposite directions (5), and many investigations in which they have been examined separately resulted in the conclusion that different etiological factors prevail at the two sites and even at the various subsites within the colon (15–17). We have examined colon and rectum cancer separately and together and have evaluated each risk separately for three subdivisions of the colon.

MATERIALS AND METHODS

The cases were consecutively diagnosed, histologically confirmed incident cases of adenocarcinoma of the colon or rectum which occurred in white male residents of Los Angeles County who were under 45 years of age at diagnosis. Patients were identified through the Los Angeles County Cancer Surveillance Program (18), a population-based tumor registry covering the entire county for all cases of cancer that are microscopically verified or mentioned on a death certificate. Efforts were made to recruit all cases diagnosed between July 1, 1974, and February 28, 1982. When the case died before an interview could be arranged, a proxy interview was conducted with the closest relative familiar with the habits and occupational history of the case.

A control was individually matched to each case on race, sex, date of birth (within 5 years), and neighborhood of residence. He was identified by an algorithm that uses the house of the index case as a reference point and proceeds in a systematic and invariable sequence until up to 80 residential units have been canvassed. Efforts were made to choose the first eligible resident in this sequence as the control. If the first eligible subject refused to participate, the second eligible subject in the sequence was asked.

At the close of case recruitment, 232 eligible patients with colorectal cancer had been identified. The attending physician refused permission for 22 patients, 30 cases could not be located in the area, and 4 cases could not speak a language for which a translator was available. Of the remaining 176 patients, case (or surrogate) interviews were conducted for 151; the remaining 25 patients (or surrogates) did not wish to participate. Finally, an eligible neighborhood control could not be located for 4 interviewed cases, leaving a total of 147 case-control pairs for study. A comparison of these 147 cases with other colorectal cases of the same age collected by the Los Angeles County Cancer Surveillance Program showed them to be representative of all eligible patients; *i.e.*, there were no statistically significant differences in their distributions by marital status, religion, birthplace, social class, or subsite.

The 147 controls were found after screening 2146 residential units, or an average of 14.6 units/control. Most of the controls were the first ($n = 112$) or second ($n = 27$) eligible neighbors. No match resided in 80.7% of the residential units canvassed, eligible but unwilling individuals lived in 2.4%, no census could be completed for 10.1%, and the 147 interviewed controls resided in the remaining 6.8%.

All interviews were conducted between April 1, 1975, and January 31, 1984, by the same interviewer and most took place in the homes of the respondents (95% of cases and 90% of controls). The remaining interviews were conducted by telephone at the request of the respondents. The median time between diagnosis and interview of the cases was 7 months; the median time between the interviews of case and matching control was 4 months. All interviews used the same structured questionnaire, designed to elicit a lifetime occupational history, vocational and avocational exposures to specific substances and industrial processes, use of tobacco and alcohol, usual consumption of foods grouped into a few broad categories, prior medical conditions, and family history of selected diseases. All events occurring after the cancer diagnosis were ignored for the case and his matching control.

Proxy interviews were conducted with the spouse for 18 cases, and a parent, a sibling, and a child responded for 4, 2, and 1 cases, respectively. An early attempt to obtain proxy interviews from the analogous member of the control family proved to be impractical; therefore only

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8 proxy interviews were conducted among the matched controls of the 25 proxy case interviews. Analyses were performed both with and without the pairs and no important differences were found; all tables therefore include the proxy interviews except for Tables 6 and 7 when it was believed *a priori* that only the subject himself was likely to be aware of the specific job exposures.

Some forms of colon cancer have an hereditary component and/or predisposing medical condition, especially those occurring early in life (19, 20). Twelve cases (and one control) in this series reported at least 1 first degree relative with large bowel cancer; 2 of these had multiple polyposis as well. Another 6 cases (and no control) gave a history of chronic colon disease: 2 with ulcerative colitis; 3 with nonulcerative colitis; and 1 with adenomatous polyps. Analyses were performed with and without these subjects and no appreciable differences were found; the reported results include these 18 cases.

Conversion factors were used to compute total ethanol intake from reported amounts of beer, wine, and spirits: 1 can of beer = 12.96 g ethanol; 1 glass of dinner wine = 10.10 g ethanol; 1 glass of sweet wine = 15.76 g ethanol; and one jigger of spirits = 14.03 g ethanol (21).

No question in the questionnaire addressed physical activity directly, since physical activity was not a hypothesis when the study was initiated. Job activity, however, was assessed in two ways. (*a*) Activity levels were inferred from job titles. All job titles were coded using the 1970 United States Bureau of Census Index of Industries and Occupations (22). Each job title in this Index had been assigned previously to one of three activity levels (9): "mainly sedentary" when physical activity is required less than 20% of the time spent on the job; "moderately active" when physical activity is required between 20 and 80% of the time; and "very active" when physical activity is required more than 80% of the time. (*b*) For colon pairs only, one of us (D. G.) blindly (with respect to case or control status) examined each questionnaire and, for each job, estimated the hours per day spent sitting, standing, or moving about; being moderately active; and being vigorously active. These judgments were based on a combination of job title, industry, employer, dates of employment, major responsibilities, and reported exposures to chemicals, dusts, and other occupational hazards. A weighted job activity score was formed by multiplying the proportion of time spent in category i (i = 1, 2, 3, and 4) by weight i, and then summing the four cross-product terms. These weights were chosen to be roughly proportional to the ratio of kilocalories normally expended at the four levels of activity (23). Since the 3-level classification system based on job titles conservatively classifies over 70% of all subjects as "moderately active," the middle level was used as the baseline category in computing ORs[3] for both methods of assessing job activity.

Occupational exposures to specific substances were examined in three ways. (*a*) Exposures were inferred from job titles alone. Each job title in the United States Bureau of Census 1970 Index had been assigned previously to one of 10 categories of particulate exposure reflecting the type(s) of dust exposure likely to occur in jobs with that title (24). (*b*) For each job in their job history, subjects were asked whether they inhaled "chemical solvents, dusts, or other fumes" and whether they routinely "got chemicals, oils, dust, etc. on their skin or clothes." When responses to either question were positive, the specific substances inhaled or contacted were elicited and coded. Finally, subjects were asked if they had ever held a job in which they were exposed to each of 23 specified substances or processes.

The pathology report for each case was examined to ascertain the subsite location of the primary lesion. Subsite analyses were based on the following groups of subsites: (*a*) right-sided (ileocecum, cecum, and ascending colon); (*b*) transverse/descending colon (hepatic flexure, transverse colon, splenic flexure, and descending colon); (*c*) sigmoid (only sigmoid); and (*d*) rectum (rectosigmoid, and other rectum).

Standard matched-pair methods (25) were used to compare interview responses between cases and their controls. Study variables were examined individually and simultaneously. The exact binomial test was used on individual dichotomous variables, and multivariate logistic regression was used for variables with more than two levels as well as for the multivariate analyses. Due to the limited number of cases at each subsite, we also examined case-control differences in various subsets of cases by comparing them with all (n = 147) controls, using cross-classification and unconditional logistic regression methods (25). Results of the stratified analysis were similar to those obtained from the matched analysis. All subsite analyses reported in this paper were based on the unconditional scheme since they provide more stable risk estimates. Subjects who failed to answer any particular question were eliminated from that analysis, as was the pair in a matched analysis when either case or control failed to answer. All reported P values are two-sided.

[3] The abbreviation used is: OR, odds ratio.

RESULTS

The cases ranged in age between 24 and 44 years, but 74% were between 35 and 44 years of age at diagnosis. Only 4 of the tumors were diagnosed at the preinvasive stage; roughly one-fifth were classified as mucinous adenocarcinoma. By primary subsite, the cases were divided as follows: 1 in the ileocecum; 19 in the cecum; 18 in the ascending colon; 6 at the hepatic flexure; 18 in the transverse colon; 6 at the splenic flexure; 13 in the descending colon; 25 in the sigmoid; 13 at the rectosigmoid; and 28 in the lower parts of the rectum.

Controls were similar to cases in their distributions by age, height, marital status, religion, birthplace, and ethnicity (Latino *versus* non-Latino). Cases tended to be less educated (P = 0.02, t test) and slightly more obese (P = 0.02) (Table 1).

Subjects were asked if, over most of their adult lives, they had eaten each of several foods or types of foods "once a week or less, 2 to 4 times a week, or 5 times a week or more." For tumors located on the right (ascending) side of the colon, elevated risks were associated with heavy consumption of deep fried foods (OR = 3.9, P = 0.008), fried bacon or ham (OR = 2.6, P = 0.08), and barbecued or smoked meats (OR = 2.9, P = 0.02) (Table 2). These associations were not seen for the other subsites of the colon. Consumption of fresh fruits and raw vegetables was inversely related to risk in the colon (P for trend = 0.006) but not the rectum; this protective effect was strongest in the transverse through descending colon (P for trend = 0.004). A preference for whole grain bread was also protective in the colon (P for trend = 0.02) but not the rectum. The only item associated with rectal cancer was deep fried food (P for trend = 0.01). Beef was not associated with risk at any of the four subsites, and no consistent pattern of risk was discernible for consumption of milk. Adjustment for Quetelet's index did not alter any of these results.

Cigarette smoking and alcohol consumption were unrelated to cancer at any of the four subsites in these young men (Table 3). Cases and controls were similarly distributed among the never smokers, exsmokers, and current smokers; neither average daily ethanol intake nor cumulative ethanol drink-years were associated with significantly increased risk at any subsite. Specific types of alcoholic beverages consumed were also examined separately, and none, including beer, was associated with excess risk.

Table 4 shows risk by job activity. When activity levels were based on the job title of the longest held job, sedentary jobs were associated with significant excess risk in the transverse/descending colon (OR = 3.0, $P < 0.05$), but not at the other colorectal subsites. The same patterns of risk prevailed when activity levels were based on the title of the most recent job, the number of years in a sedentary job, and the proportion of job history spent in a sedentary job. When job activity levels were based on tertiles of the weighted job activity scores for all jobs held between the ages of 18 and 28 years, at the time when these tumors are presumed to have been forming, we again observed an increased risk associated with job inactivity which

Table 1 *Demographic characteristics of subjects: colorectal cancer, Los Angeles County*

Characteristic	Controls [All (n = 147)]	Cases				
		All (n = 147)	Right-sided (n = 38)	Transverse/ descending (n = 43)	Sigmoid (n = 25)	Rectum (n = 41)
Age at diagnosis (yr)	38.2 ± 5.7[a]	38.5 ± 5.2	38.5 ± 4.8	38.8 ± 4.9	38.2 ± 5.3	38.5 ± 5.8
Yr of education	14.5 ± 3.2	13.7 ± 2.7[b]	13.9 ± 2.7	13.8 ± 3.1	13.1 ± 2.6[b]	13.8 ± 2.4
Height (cm)	180.0 ± 7.3	179.0 ± 7.8	178.6 ± 10.0	179.2 ± 7.6	178.9 ± 6.4	179.2 ± 6.6
Wt 1 yr ago (kg)	81.3 ± 12.4	83.5 ± 13.4	83.3 ± 13.4	82.0 ± 14.5	85.0 ± 13.1	84.2 ± 12.7
Quetelet's index[c]	25.0 ± 3.4	26.0 ± 3.7[b]	26.2 ± 4.5	25.4 ± 3.5	26.5 ± 3.3	26.1 ± 3.2
Married (%)	77.6	76.2	71.1	79.1	72.0	80.5
Hispanic white (%)	6.8	10.9	7.9	9.3	16.0	12.2
Catholic (%)	27.9	32.7	34.2	25.6	32.0	39.0
Protestant (%)	40.1	42.2	47.4	41.9	44.0	36.6

[a] Mean ± SD.
[b] $P < 0.05$ (t test for comparison with all controls).
[c] Weight (kg) 1 year ago, divided by height (meters) squared.

Table 2 *Risk by subsite for usual consumption of specified foods (over most of adult life): colorectal cancer, Los Angeles County*

Times eaten/wk	Cases/ controls	OR[a] (95% CI)[b] [All cases (n = 147)]	OR[c] (95% CI)			
			Right side (n = 38)	Transverse/ descending (n = 43)	Sigmoid (n = 25)	Rectum (n = 41)
Deep fried foods						
≤1	71/81	1.0	1.0	1.0	1.0	1.0
2–4	51/55	1.0 (0.6, 1.8)	0.8 (0.3, 1.9)	0.8 (0.4, 1.7)	1.2 (0.5, 3.0)	1.4 (0.6, 3.0)
≥5	25/11	2.1 (1.0, 4.6)	3.9 (1.4, 10.7)	1.2 (0.4, 4.2)	1.1 (0.2, 5.6)	4.3 (1.5, 12.1)
Fried bacon or ham						
≤1	89/85	1.0	1.0	1.0	1.0	1.0
2–4	45/51	0.8 (0.5, 1.3)	1.0 (0.5, 2.3)	0.8 (0.4, 1.6)	0.5 (0.2, 1.4)	0.9 (0.4, 2.0)
≥5	13/11	1.0 (0.4, 2.4)	2.6 (0.9, 7.9)	0.2 (0.02, 1.7)	0.0 (—)	1.5 (0.4, 4.8)
Barbecued or smoked meats						
≤1	125/130	1.0	1.0	1.0	1.0	1.0
2–4	20/16	1.3	2.9	1.1	1.0	0.8
≥5	2/1	(0.6, 2.7)	(1.2, 7.3)	(0.4, 3.1)	(0.3, 3.8)	(0.3, 2.7)
Beef						
≤1	3/7	1.0	1.0	1.0	1.0	1.0
2–4	59/54					
≥5	85/86	1.0 (0.6, 1.6)	1.0 (0.5, 2.0)	0.9 (0.4, 1.7)	1.1 (0.4, 2.6)	1.1 (0.6, 2.3)
Fresh fruits or raw vegetables (e.g., salads)[d]						
≤1	15/10	1.7 (0.7, 4.1)	1.6 (0.4, 6.7)	4.0 (1.3, 12.3)	1.7 (0.4, 7.9)	0.5 (0.1, 2.5)
2–4	46/37	1.8 (1.0, 3.1)	2.0 (0.9, 4.7)	2.7 (1.2, 6.1)	1.6 (0.6, 4.4)	0.6 (0.3, 1.6)
≥5	75/99	1.0	1.0	1.0	1.0	1.0
Bread preference						
White	78/64	1.0	1.0	1.0	1.0	1.0
None	30/32	0.8 (0.4, 1.4)	0.4 (0.1, 1.2)	0.7 (0.3, 1.7)	1.1 (0.4, 3.2)	1.5 (0.6, 3.6)
Whole grain	39/51	0.6 (0.4, 1.1)	0.6 (0.3, 1.4)	0.5 (0.2, 1.2)	0.7 (0.2, 1.9)	1.0 (0.4, 2.3)
Milk						
≤1	34/40	1.0	1.0	1.0	1.0	1.0
2–4	27/18	1.6 (0.8, 3.3)	1.3 (0.4, 4.0)	2.9 (1.0, 8.2)	0.4 (0.1, 2.4)	2.1 (0.6, 7.4)
≥5	86/89	1.0 (0.6, 1.8)	0.8 (0.3, 1.8)	1.0 (0.4, 2.4)	0.7 (0.3, 1.9)	2.1 (0.8, 5.4)

[a] Adjusted for education, age was a matching variable.
[b] CI, confidence interval.
[c] Adjusted for age and education in analyses using all controls.
[d] Numbers do not sum to 147 since this item was added after 11 cases and 1 control had already been interviewed.

Table 3 *Risk by subsite for cigarette smoking and alcohol intake: colorectal cancer, Los Angeles County*

	Cases/ controls	OR[a] (95% CI)[b] [all cases (n = 147)]	OR[c] (95% CI) Colon (n = 106)	OR[c] (95% CI) Rectum (n = 41)
Cigarette smoking				
Never	48/43	1.0	1.0	1.0
Exsmoker	34/38	0.7 (0.4, 1.4)	0.6 (0.3, 1.3)	0.7 (0.3, 1.8)
≤1 pack/day	23/27	0.7 (0.3, 1.4)	0.4 (0.2, 1.0)	0.9 (0.3, 2.5)
2+ packs/day	38/30	0.9 (0.4, 1.8)	1.1 (0.5, 2.1)	0.5 (0.2, 1.5)
Daily ethanol intake (g)				
0–9	61/63	1.0	1.0	1.0
10–39	39/38	1.0 (0.5, 1.8)	1.0 (0.5, 1.9)	1.2 (0.5, 2.7)
40–69	25/33	0.7 (0.4, 1.3)	0.8 (0.4, 1.5)	0.6 (0.2, 1.8)
70+	20/12	1.6 (0.7, 3.7)	1.6 (0.6, 3.7)	1.4 (0.4, 4.5)
Years drank beer at least once/wk				
0	56/59	1.0	1.0	1.0
1–9	18/21	0.9 (0.4, 1.8)	0.9 (0.4, 2.0)	0.7 (0.2, 2.4)
10–19	37/35	1.1 (0.6, 2.1)	1.0 (0.5, 1.8)	1.5 (0.6, 3.5)
≥20	34/32	0.9 (0.5, 1.8)	1.0 (0.5, 2.0)	0.9 (0.3, 2.3)

[a] Adjusted for education; age was a matching variable.
[b] CI, confidence interval.
[c] Adjusted for age and education in analyses using all controls.

was specific for the transverse/descending colon. Similar results were obtained when the analysis was based on the weighted job activity scores of the most recent job, the longest held job, and the entire job history.

Table 5 shows risk by exposure to any job judged to be dusty on the basis of its job title. Throughout the colorectum, having ever held a dusty job was associated with a modest excess risk (OR = 1.7; $P = 0.07$); there were significant dose-response relationships with both the number of years in a dusty job and the interval since the first dusty job. The excess risk was strongest in the rectum (OR = 2.1; $P = 0.09$), followed closely by the sigmoid (OR = 1.9; $P = 0.25$); there was no excess risk in the midsection of the colon and a small excess in the cecum/ascending colon (OR = 1.6; $P = 0.26$). This same pattern of risk persisted for exposure to most of the specific types of dust, but the greatest excess risks were associated with organic and metal dusts, for which there were 3-fold excess risks in the rectum ($P = 0.03$ and 0.03 for organic and metal dusts, respectively).

Table 6 shows the risk associated with several job characteristics (excluding proxy interviews). There was no excess risk associated with getting chemicals on one's skin/clothes, but for tumors of the rectum, there was an almost 4-fold excess risk ($P = 0.04$) for ever inhaling dusts or fumes on a job. Also for rectal cancer, there were significant dose-response relationships with both the years on jobs in which dust or fumes were inhaled ($P = 0.04$) and the interval since the first such job ($P = 0.045$). Over 90% of these dust/fume-exposed tumors occurred at least 10 years after this first exposure. There was also a 2-fold elevation in risk ($P = 0.28$) of sigmoid cancer after 10 or more years of inhaling dusts/fumes. Tumors located above the sigmoid were not associated with inhaling dusts/fumes, except, possibly, 20 years after the first exposure.

Substances described by subjects as inhaled on a job were grouped first as particulates (dusts and metal fumes) and nonparticulates (vapors and gases) and then by type of substance within each category. In the rectum, moderate but nonsignificant excess risks were associated with both particulates (OR = 3.4, $P = 0.06$) and nonparticulates (OR = 3.0, $P = 0.09$). Examination of specific types of dust indicated that the risk of rectal cancer was highest for wood dust (OR = 9.4, $P = 0.005$) (Table 6). Other organic dusts showed no clear association with rectal cancer, but there were nonsignificant elevations in risk for metal (OR = 2.4, $P = 0.26$) and mineral dusts (OR = 3.0, $P = 0.14$). No specific type of nonparticulates explained the elevated risk for rectal cancer associated with inhaling vapors and gases.

In the sigmoid colon, the pattern of risk associated with self-described particulates closely resembled that in the adjacent rectum, but the risk estimates in the sigmoid were not as high and none was statistically significant (Table 6). Moderately elevated risks were present for both wood (OR = 3.6, $P = 0.16$) and metal dusts (OR = 2.0, $P = 0.38$). The only exposure for which the pattern of risk was not similar between the rectum and sigmoid was to nonwood organic dusts (OR = 3.2 in the sigmoid and 1.2 in the rectum); these included textile dust, soil, and nonspecific household dust. In the right, transverse, and descending colon there was no significant association with any inhaled dust or gas, but the risks for all organic dusts were somewhat elevated.

When subjects were asked directly about 23 specific substances and industrial processes, only nonferrous metal exposure was significantly associated with sigmoid cancer (OR = 3.0, $P = 0.03$) (Table 7). Review of the metals involved did not implicate a specific metal; aluminum, lead, beryllium, copper, tin, zinc, titanium, and molybdenum were all represented. Ex-

Table 4 *Risk by subsite for job activity: colorectal cancer, Los Angeles County*

	Cases/ controls	OR[a] (95% CI)[b] [all cases (n = 147)]	OR[c] (95% CI) Right side (n = 38)	Transverse/ descending (n = 43)	Sidmoid (n = 25)	Rectum (n = 41)
Activity level of longest held job						
Mainly sedentary	28/21	1.7 (0.9, 3.4)	1.0 (0.3, 3.1)	3.0 (1.2, 7.2)	1.7 (0.5, 6.0)	1.5 (0.6, 4.0)
Moderately active	101/109	1.0	1.0	1.0	1.0	1.0
Very active	18/17	1.1 (0.5, 2.3)	1.0 (0.3, 3.2)	0.8 (0.2, 2.7)	1.6 (0.5, 5.1)	0.7 (0.2, 2.5)
Tertiles of weighted job activity score for ages 18 through 28 yr[d]						
1st (least active)	30/35	0.8 (0.4, 1.6)	0.7 (0.3, 1.7)	1.6 (0.7, 4.1)	0.2 (0.04, 1.1)	
2nd	42/35	1.0	1.0	1.0	1.0	
3rd (most active)	34/36	0.8 (0.4, 1.5)	0.5 (0.2, 1.2)	0.9 (0.4, 2.3)	1.0 (0.4, 2.7)	

[a] Adjusted for education; age was a matching variable.
[b] CI, confidence interval.
[c] Adjusted for age and education in analyses using all controls.
[d] Score was not computed for cases of rectum cancer and their matched controls.

Table 5 *Risk by subsite for exposure to dusty jobs (as inferred from job titles): colorectal cancer, Los Angeles County*

	Cases/ controls	OR[a] (95% CI)[b] [all cases (n = 147)]	OR[c] (95% CI) Right side (n = 38)	Transverse/ descending (n = 43)	Sidmoid (n = 25)	Rectum (n = 41)
Ever held a dusty job						
No	39/57	1.0	1.0	1.0	1.0	1.0
Yes	108/90	1.7 (1.0, 2.9)	1.6 (0.7, 3.8)	1.0 (0.5, 2.1)	1.9 (0.6, 5.8)	2.1 (0.9, 5.0)
Years held a dusty job						
1–9	55/51	1.6 (0.9, 2.8)	1.4 (0.6, 3.6)	1.1 (0.5, 2.4)	1.9 (0.6, 6.1)	2.0 (0.8, 4.9)
10+	53/39	2.0 (1.0, 4.0)	2.1 (0.7, 5.8)	0.8 (0.3, 2.3)	2.0 (0.5, 7.2)	2.4 (0.9, 6.7)
Test for trend (P)		0.05	0.16	>0.50	0.32	0.09
Years since first held a dusty job						
1–9	5/10	0.3 (0.1, 1.8)	0.8 (0.1, 4.8)	0.0 (—)	0.8 (0.1, 9.7)	1.2 (0.2, 7.8)
10–19	40/30	1.7 (0.9, 3.4)	0.9 (0.3, 3.0)	1.4 (0.5, 3.7)	2.5 (0.7, 9.4)	2.4 (0.8, 6.9)
20+	63/50	1.9 (1.0, 3.6)	2.3 (0.9, 6.0)	0.9 (0.4, 2.2)	1.8 (0.5, 6.1)	2.1 (0.8, 5.4)
Test for trend (P)		0.03	0.10	>0.50	0.26	0.09
Type of dust on dusty job						
Organic dust	39/30	1.8 (0.9, 3.8)	1.7 (0.6, 5.0)	0.5 (0.2, 1.7)	2.1 (0.6, 8.0)	3.0 (1.1, 8.6)
Metal dust	47/34	1.9 (1.0, 3.9)	1.1 (0.4, 3.5)	0.9 (0.3, 2.5)	2.7 (0.8, 9.5)	3.0 (1.1, 8.0)
Mineral dust	27/26	1.4 (0.7, 3.0)	1.4 (0.4, 4.3)	0.8 (0.2, 2.3)	1.5 (0.4, 6.3)	1.7 (0.6, 5.4)
Smoke or exhaust	18/21	1.2 (0.5, 2.6)	1.4 (0.4, 4.8)	0.4 (0.1, 1.7)	1.5 (0.3, 6.8)	1.3 (0.4, 4.8)
Unknown dust	70/60	1.6 (0.9, 2.9)	1.8 (0.8, 4.4)	1.0 (0.4, 2.2)	1.5 (0.4, 4.9)	2.1 (0.8, 5.2)

[a] Adjusted for education using "never dusty job" as reference group; age was a matching variable.
[b] CI, confidence interval.
[c] Adjusted for age and education in analyses using all controls and "never dusty job" as reference group.

posure to nonferrous metals was also somewhat associated with rectal cancer, but this OR was not statistically significant (OR = 2.0, P = 0.08). Interestingly, exposure to ferrous metals showed no association with cancer at any site in the colon or rectum. Wood dust when asked as a specific item was associated with sigmoid and rectum cancer, but not significantly, and not as strongly as when subjects were asked to name the substances they inhaled on specific jobs.

Direct questions were also asked about leisure time exposure to 17 specified substances. No significantly elevated risks were found in association with any of these substances.

Multivariate analyses demonstrated that the findings for the dietary factors (deep fried foods, fresh fruits or raw vegetables, and bread preference), for physical activity, and for occupational exposure to dusts/fumes were not confounded by each other; *i.e.*, the ORs for each of these variables were not substantively altered after adjustment for the other variables. Similarly, adjustment of these same variables for Quetelet's index did not substantively alter any of these risk estimates.

DISCUSSION

Analytical studies of colorectal cancer have revealed associations with exposures which have been diverse, often inconsistent, and usually of relatively small magnitude. In this study of colorectal cancer in young men, we observed several rather strong associations, particularly when restricting the focus to specific segments of the large bowel. Consumption of fresh fruits and raw vegetables and a preference for whole grain breads were protective throughout the colon but not in the rectum; fatty foods increased risk at both proximal and distal ends of the colorectum but not at the intervening subsites; and barbecued/cured meats increased risk only in the right colon. Occupational physical activity was protective in the midsections of the colon (transverse/descending subsites) but not in the more proximal or distal segments of the colorectum. Tumors in the rectum and to a lesser degree the sigmoid were associated with dusty jobs. This latter effect was somewhat nonspecific; *i.e.*, all types of dusts and fumes increased risk to some degree. However, wood and metal dust conveyed the greatest risk in both the rectum and the adjacent sigmoid. Beef, milk, alcohol, and cigarette smoking appeared to play little or no role in the etiology of these tumors at any subsite. Perhaps more importantly, however, this case-control study of colorectal cancer in young men does not support the hypothesis that different subsites of the colorectum share the same environmental risk factors.

Because this study was limited to young cases, the findings may not be generalizable to bowel cancers arising in older subjects. Tumors occurring early in life may be more likely to have a hereditary component and/or a predisposing medical condition and may represent a different spectrum of disease than those which occur later in life. Nonetheless, we found no important differences in levels of risk when our analyses excluded cases with a family history of colorectal cancer and/or chronic colitis. Furthermore, all exposures associated with bowel cancer in this study have been reported in previous studies which included youthful cases as a small fraction of the subjects if at all.

On the other hand, a study limited to young cases does have special advantages. The interval between exposure and disease onset is comparatively short, and thus recall of past experience is relatively accurate. Such a short interval may also reflect a

Table 6 *Risk by subsite for job characteristics and job exposures described by subjects (self-respondents only): colorectal cancer, Los Angeles County*

	Cases/ controls	OR[a] (95% CI)[b] [all cases (n = 147)]	OR[c] (95% CI) Right side (n = 38)	Transverse/ descending (n = 43)	Sigmoid (n = 25)	Rectum (n = 41)
Every held job in which "chemicals, oils, or dusts got on skin or clothes"						
No	45/52	1.0	1.0	1.0	1.0	1.0
Yes	77/87	1.0 (0.6, 1.7)	0.8 (0.3, 1.7)	0.7 (0.3, 1.6)	1.2 (0.4, 3.9)	1.0 (0.5, 2.3)
Ever held job in which "chemicals, dust, or fumes were inhaled"						
No	20/35	1.0	1.0	1.0	1.0	1.0
Yes	102/104	1.5 (0.8, 3.0)	1.1 (0.4, 2.8)	1.1 (0.4, 2.9)	1.4 (0.4, 5.4)	3.8 (1.1, 13.6)
Years in a job in which chemicals, dust, or fumes were inhaled						
0	20/35	1.0	1.0	1.0	1.0	1.0
1–9	51/50	1.6 (0.8, 3.2)	1.4 (0.5, 3.8)	1.5 (0.6, 4.1)	0.8 (0.2, 3.8)	3.4 (0.9, 12.9)
10+	51/54	1.5 (0.7, 3.2)	0.8 (0.3, 2.4)	0.7 (0.2, 2.2)	2.2 (0.5, 9.4)	4.3 (1.1, 16.5)
Test for trend (P)		0.38	>0.50	0.43	0.17	0.04
Years since first job in which chemicals, dust, or fumes were inhaled						
0	20/35	1.0	1.0	1.0	1.0	1.0
1–9	6/16	0.3 (0.1, 1.3)	0.3 (0.1, 2.1)	0.2 (0.02, 2.0)	0.0 (—)	1.8 (0.3, 11.1)
10–19	41/38	1.7 (0.7, 4.0)	0.8 (0.2, 2.5)	1.1 (0.4, 3.4)	1.6 (0.4, 7.1)	4.9 (1.3, 18.4)
20+	55/50	1.7 (0.8, 3.8)	1.8 (0.6, 5.5)	1.5 (0.5, 4.4)	2.4 (0.5, 12.3)	3.4 (0.9, 13.7)
Test for trend (P)		0.06	0.28	0.33	0.16	0.045
Substances described as inhaled on a job						
Dusts or metal fumes	71/73	1.6 (0.8, 3.3)	0.9 (0.3, 2.6)	1.1 (0.4,2 .9)	1.7 (0.4, 6.9)	3.4 (0.9, 12.6)
Organic dusts	32/19	2.6 (1.1, 6.3)	2.1 (0.6, 6.6)	1.5 (0.4, 5.2)	3.4 (0.7, 15.4)	5.2 (1.2, 22.1)
Wood dust	21/10	3.6 (1.2, 11.0)	2.1 (0.5, 8.5)	1.5 (0.3, 6.6)	3.6 (0.6, 20.5)	9.4 (2.0, 44.7)
Other organic dust	11/9	1.9 (0.6, 5.5)	2.1 (0.5, 8.7)	1.6 (0.3, 7.4)	3.2 (0.5, 19.3)	1.2 (0.1, 13.5)
Metal dusts	24/27	1.2 (0.5, 2.9)	0.8 (0.2, 2.8)	1.0 (0.3, 3.3)	2.0 (0.4, 9.5)	2.4 (0.5, 10.8)
Mineral dusts	26/30	1.4 (0.6, 3.2)	1.0 (0.3, 3.4)	0.9 (0.3, 3.1)	1.3 (0.3, 6.7)	3.0 (0.7, 12.6)
Vapors or gases	89/100	1.3 (0.6, 2.6)	1.0 (0.4, 2.5)	1.0 (0.4, 2.7)	1.3 (0.3, 5.2)	3.0 (0.8, 10.9)

[a] Adjusted for education; age was a matching variable.
[b] CI, confidence interval.
[c] Adjusted for age and education in analyses using all controls.

single unusually intense exposure, and therefore perhaps a predominant causal element.

Recall bias is not likely to have produced the positive findings. The interviewer followed the same structured questionnaire and used the same probes and follow-up questions with all subjects [and indeed with subjects in several other cancer case-control studies conducted simultaneously (26–30)]. If cases had systematically recalled more exposures than controls, findings would not have been so site specific or exposure specific. Laymen generally fail to distinguish between cancers at different sites, much less between cancers at subsites within the large bowel. Some exposures conventionally linked with cancer, namely, smoking, beef, alcohol consumption, and direct chemical contact, were not associated with elevated risk at any subsite. Finally, a number of specific exposures were, if anything, inversely associated with risk.

The positive occupational findings were generally consistent over the different methods of assessing exposure. Inferring exposure from job titles offers objectivity and freedom from bias, but it may result in substantial misclassification. Nonetheless, exposures to both organic and metal dusts were significantly associated with rectal cancer using this method of assigning exposure. When subjects were asked to name the specific exposures associated with their jobs, organic and metal dusts were again associated with rectal cancer, although only the former association was statistically significant. Exposure to wood dust was primarily responsible for this association between organic dust and rectal cancer. As it turned out, almost 70% of the subjects were classified the same way by job title and self-report, and the strengths of the observed risks were enhanced when the analysis was limited to this subset. The third method of assessing exposure, *i.e.*, asking subjects to review lists of specific exposures, is designed to minimize the recall bias inevitably associated with volunteered reports but tends to overestimate less salient exposures. This it is not surprising that the associations with both organic and metal dusts were weakest when exposures were assessed by this third method.

We observed a small association with obesity, and this association was relatively consistent over the subsites of the colorectum. Other case-control studies have reported cases to be both more (12, 31, 32) and less (33, 34) obese than controls.

Table 7 *Risk by subsite for occupational exposure to prespecified substances and processes (self-respondents only): colorectal cancer, Los Angeles County*

	Cases/ controls	OR[a] (95% CI)[b] [all cases (n = 147)]	OR[c] (95% CI)			
			Right side (n = 38)	Transverse/ descending (n = 43)	Sigmoid (n = 25)	Rectum (n = 41)
Wood dust	28/26	1.2 (0.6, 2.3)	1.1 (0.4, 2.9)	0.6 (0.2, 1.8)	1.9 (0.6, 5.7)	1.4 (0.6, 3.4)
Grain dust	10/7	1.9 (0.6, 5.6)	2.5 (0.7, 9.2)	0.5 (0.1, 4.0)	3.2 (0.7, 14.4)	0.9 (0.2, 4.9)
Any metal dusts or fumes	42/43	1.1 (0.6, 1.9)	0.6 (0.2, 1.4)	0.7 (0.3, 1.7)	2.0 (0.7, 5.5)	1.7 (0.8, 3.7)
Ferrous metals	21/25	0.8 (0.4, 1.7)	0.6 (0.2, 1.8)	0.7 (0.2, 2.0)	1.1 (0.3, 3.7)	1.1 (0.5, 2.8)
Nonferrous metals	38/34	1.3 (0.8, 2.4)	0.7 (0.3, 1.8)	0.9 (0.4, 2.2)	3.0 (1.1, 8.2)	2.0 (0.9, 4.2)
Cutting, cooling, lubricating oils	40/42	1.1 (0.6, 2.0)	0.9 (0.4, 2.2)	0.9 (0.4, 2.2)	0.8 (0.3, 2.6)	1.1 (0.5, 2.4)
Asbestos	14/20	0.8 (0.4, 1.7)	0.4 (0.1, 1.6)	0.5 (0.1, 1.8)	1.5 (0.4, 5.0)	0.8 (0.3, 2.4)
Fibrous glass or glass wool	19/36	0.4 (0.2, 0.8)	0.4 (0.2, 1.3)	0.5 (0.2, 1.3)	0.5 (0.1, 1.8)	0.4 (0.1, 1.1)
Pesticides	12/22	0.6 (0.3, 1.3)	0.5 (0.1, 1.9)	0.3 (0.1, 1.4)	0.6 (0.1, 2.9)	0.8 (0.3, 2.3)
Wood preservatives	6/12	0.5 (0.2, 1.4)	0.0 (—)	0.6 (0.1, 2.9)	1.3 (0.3, 6.5)	0.6 (0.1, 2.7)
Paints and lacquers	37/43	1.0 (0.6, 1.8)	0.7 (0.3, 1.6)	1.1 (0.5, 2.4)	0.7 (0.2, 2.3)	1.0 (0.4, 2.1)
Spray paints	27/44	0.6 (0.3, 1.1)	0.3 (0.1, 1.0)	0.4 (0.1, 1.1)	0.7 (0.2, 2.1)	0.8 (0.4, 1.8)
Petroleum products	45/51	1.0 (0.6, 1.7)	0.7 (0.3, 1.7)	0.9 (0.4, 2.1)	1.0 (0.3, 2.7)	1.1 (0.5, 2.2)
Organic solvents	67/68	1.3 (0.7, 2.2)	0.9 (0.4, 2.1)	1.3 (0.6, 2.9)	1.4 (0.5, 4.0)	1.1 (0.5, 2.3)
Coal tar, soot, pitch	13/19	0.8 (0.4, 1.7)	0.6 (0.2, 2.3)	1.0 (0.3, 2.9)	0.3 (0.04, 2.8)	0.7 (0.2, 2.3)
Arsenic	6/6	1.4 (0.4, 5.0)	1.6 (0.3, 8.2)	0.0 (—)	3.1 (0.5, 16.9)	1.3 (0.3, 6.8)
Dyestuffs	17/15	1.5 (0.7, 3.4)	1.5 (0.5, 4.4)	1.0 (0.3, 3.3)	3.9 (1.2, 12.1)	0.4 (0.1, 2.0)
Plastics processing	15/16	1.1 (0.5, 2.6)	1.5 (0.5, 4.4)	1.1 (0.3, 3.4)	0.5 (0.1, 3.9)	1.2 (0.4, 3.4)
Rubber processing	6/7	1.1 (0.3, 4.0)	1.3 (0.3, 6.7)	0.0 (—)	2.7 (0.5, 14.4)	1.1 (0.2, 5.7)

[a] Adjusted for education; age was a matching variable.
[b] CI, confidence interval.
[c] Adjusted for age and education in analyses using all controls.

The observed protection against colon cancer associated with dietary fruits, raw vegetables, and whole grain bread is consistent with previous case-control studies (35–38). The risk conveyed by deep fried foods is consistent with elevated risks from fat intake (17, 32–34, 39), and the elevated risk of cecum and ascending colon cancer after cured/barbecued meat consumption is consistent with the hypothesis that *N*-nitroso compound formation increases risk (36, 40).

The association between colorectal cancer and consumption of alcohol, especially beer, has been widely studied, and while some investigators have found a moderate excess risk for heavy alcohol consumption (12, 35, 41, 42), especially for rectal cancer after heavy consumption of beer (43–45), others have found none (46–49). While we found no significant excess risk associated with any specific beverage, with derived indices of daily ethanol intake, or with cumulative drink-years, the level of association between rectal cancer risk and heavy alcohol consumption was at least consistent with a small excess risk, even though heavy or long term beer consumption did not explain it. If the previously observed relationship is real, the subjects in this study may have been too young for the cumulative effects of beer or alcohol to become manifest.

The absence of a smoking effect for either colon or rectal cancer is consistent with the findings of most other studies (36, 41, 46, 50, 51).

The initial report of a protective effect for colon cancer from physical activity on the job was based on cases from Los Angeles County (9); this finding has since been reproduced in several other settings using different study designs (10–12, 52–54). While three-fourths of the cases in the present case-control study comprise 23% of the cases in the initial report who were under age 45 years at diagnosis, it should be noted that the initial descriptive study found the protective effect for job activity to be strongest in men over the age of 45 years; in men under age 45 years, the protective effect was present only among those residing in lower socioeconomic neighborhoods. The present trend of increasing risk for cancers of the middle bowel with decreasing activity and the absolute magnitude of risk at that subsite are consistent with both the original and subsequent reports.

Wood dust is a known cause of nasal cancer (55–57) and has been associated with lung, stomach, and bladder cancers in some but not all studies (55, 58, 59). A higher risk for colorectal cancer was observed in three independent cohort studies of woodworkers in the automotive industry (6–8); a screening survey in the same industry found a higher prevalence of colorectal polyps among pattern and model makers compared to other workers (60). While an excess of rectal but not colon cancer was linked to the lumber and wood products industry in the Third National Cancer Survey Interview (16), cohort studies of carpenters and furniture workers (56, 61) have failed to find an excess risk for colorectal cancer; and the large American Cancer Society (ACS) cohort study found a reduced incidence of colorectal cancer among woodworkers, defined as carpenters,

sawmill operators, furniture makers, or one of 30 other wood-related occupations (58). The ACS investigators did observe significant excess risks for lung, stomach, and bladder cancer as well as nasal cancer, while excess risk was found only for nasal cancer in the cohort studies of carpenters and furniture workers. This study differs from previous studies not only in the youth of the cases and in the case-control design but also in that exposure to wood dust was not based on job title alone. The strongest excess risk was found for the rectum and when subjects volunteered wood dust as a substance inhaled on a job. The comparable exposure derived only from job title provided a similar statistically significant pattern of excess risk for organic dust.

For many years investigators have been reporting excess colorectal cancer in metal workers, *e.g.*, machinists, millwrights, sheetmetal workers, grinders, coppersmelters, tool and die makers, metal polishers and platers, nickel refiners, and metal frame makers (5, 16, 62–71). More recent studies have reported these associations for rectal but not colon cancer (72–74). In this study, excess risk for metal dust was observed using all three methods of assessing exposure and appeared to be restricted to the rectum and sigmoid. Most previous studies have attempted to explain these associations on the basis of the cutting oils and/or abrasives used in metal work rather than the metal dust itself. We found no excess risk associated with self-reported exposure to "cutting, cooling, or lubricating oils" but we did not ask specifically about exposure to abrasives. Such substances, however, were rarely mentioned among the dusts which were inhaled on specific jobs.

We found no elevated risk after exposure to asbestos. This does not support the 2- to 3-fold excess risk observed by Selikoff and others (3, 4, 75, 76) but is in accord with the conclusions of recent reviewers who concluded that the bulk of the evidence from both epidemiological and animal studies does not support an association between asbestos exposure and colorectal cancer (77, 78). However, few of our subjects held jobs in which asbestos exposure would have been heavy, and this study had low power to detect such an association.

We also found no association between exposure to pesticides and either colon or rectal cancer and thus fail to confirm the association suggested by investigators in the Mississippi River Valley where adolescent patients with this disease were noted to have had heavy childhood exposures to agricultural herbicides and pesticides (13, 14, 79, 80). However, our cases were urban and we did not ask about exposures during early childhood.

Abundant evidence of subsite-specific differences in bowel cancer risk has long been available, but the presumption of a common etiology is convenient and has been justified by a wish for parsimony in the face of an incomplete understanding of carcinogenesis. Still, as more evidence of physiological variation within the large bowel accumulates (81), the proposition that bowel cancer etiology is uniform becomes less plausible.

The cecum and the ascending and proximal transverse colon derive from the embryonic midgut; the distal transverse, descending, and sigmoid colon is derived from the hindgut; and the rectum and the anal canal from the cloaca. The three subdivisions have correspondingly different blood supplies, and their different patterns of motility suggest different physiological functions. Retrograde peristalsis in the upper colon churn and mix the liquid stool (81), and it is in that region that the traffic of materials into and out of the lumen is greatest. In the middle colon, rings of contraction separate the stool into roughly equivalent aliquots (82), and periodic mass propulsive movements (83, 84), related to physical activity (85), deliver stool toward the sigmoid. The lower colon and rectum are capable of distension and serve a reservoir function between powerful defecatory contractions (86). Other subsite variations which must bear on the degree of contract between stool elements and mucosal cells include luminal geometry, variations in the impact of gravity, and the subsite-specific composition of protective mucus (87).

Our findings are consistent with the existence of subsite-specific mechanisms of carcinogenesis which parallel these physiological differences. Excess risk in the upper colon was associated with animal fat, consistent with the hypothesis that 3-ketosteroids are carcinogenic, and the increased mucosal contact and absorption in that segment. Physical activity exerts a more profound effect upon transit time, as well as upon risk, in the middle colon; the reduction in risk there associated with fruit and vegetable consumption may have a related explanation, based on the effect of increased dietary fiber. Air-borne dust particles are swallowed in mucus from the respiratory tract and may therefore contact the gastrointestinal mucosa at any site. The duration of contact with any particular cell in the upper colon is probably short, even though transit time through the cecum is relatively long. In the lower bowel, the other site of long transit time, there is little churning and mixing of the relatively solid stool, and prolonged contact is a distinct possibility, particularly if particulates are nonabsorbable. It is also possible that the transit of particulates of high density, such as metal particles, is unusually slow through portions of the gastrointestinal tract where flow is reduced generally by anatomic or physiological means (88). This hypothesis is offered because in concurrent studies of carcinoma at other gastrointestinal sites, using the same instrument, we have observed increased risk in relation to metal dust in the lower esophagus (30) and in the pylorus.[4]

It is quite possible that subsite-specific variation in environmental carcinogenicity is responsible for some inconsistency between the findings of past observational studies, especially since measurement errors in the exposure indices are likely to be large. Future studies of large bowel cancer should certainly examine results by subsite as a routine procedure.

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