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Shift work, occupation and coronary heart disease over 6 years of follow-up in the Helsinki Heart Study

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Objectives The risk of coronary heart disease (CHD) in shift work and the possible pathways for CHD in industrial workers were studied along with the importance of shift work as an occupational class gradient of CHD risk.

Methods Data from a psychosocial questionnaire and on life-style factors, blood pressure, and serum lipid levels were used for a follow-up study of a cohort of 1806 workers. CHD was determined from official Finnish registers. Cox's proportional hazards models were used with different covariates to evaluate the relative risks associated with shift work.

Results All the blue-collar workers smoked more and had higher systolic blood pressure than the white-collar workers. Three-shift workers scored low for job-decision latitude on the Karasek job stress scales. There were no differences in the total cholesterol or high-density lipoprotein cholesterol levels. When all the shift workers were compared with all the day workers, the relative risk of CHD was 1.5 [95% confidence interval (95% CI) 1.1—2.1] when only age was adjusted for and 1.4 (95% CI 1.0—1.9) when life-style factors, blood pressure, and serum lipids were also adjusted for. The blue-collar day workers and 2-shift and 3-shift workers had relative risks of 1.3 (95% CI 0.8—2.0), 1.9 (95% CI 1.1—3.4), and 1.7 (95% CI 1.1—2.7), respectively, when compared with the white-collar day workers.

Conclusions Shift work is an important part of the occupational gradient in CHD risk among industrial workers; some evidence was found for the hypothesis that a direct stress-related mechanism explains part of the increased CHD risk.

Key terms blood pressure, coronary heart disease, job stress, life-style, occupation, shift work.

While most occupational health hazards have been strongly curtailed in Western industrialized countries, shift work remains common. In fact, the number of shift workers has even increased in some branches of industry, for example, in manufacturing (1). The total number of night and shift workers seems to be between some 15% and 20% of the total working population in most European Community countries (1). Approximately 20% of shift workers are forced to move to day work during their first year of employment due to disturbances in their circadian rhythm, with accompanying sleep disturbances, difficulties in social life, and various stress reactions (2). Even those who accommodate may nevertheless be at increased risk of long-term health hazards. Whether or not shift workers are at increased risk of coronary heart disease (CHD) has been studied since the

middle of the century with contrasting findings. In 1978 Harrington (3) concluded in his review that there was no conclusive evidence for an increased incidence of cardiovascular disorders for shift workers. After the follow-up study of Knutsson et al (4) and the massive aggregated data study by Alfredsson et al (5), Waterhouse and his colleagues (6) found, in their review from 1992, that the evidence in favor of an increased risk of CHD in association with shift work is becoming more difficult to dismiss than was the case in 1978.

As shift work is more common in blue-collar than in white-collar occupations and a shift-work job is rarely identical to a corresponding day work job, differences in the CHD risk between shift work and day work are closely linked to differences in risk between occupational groups. Since the Black report (7) several studies in

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different countries have explored differences in CHD mortality and morbidity between occupational groups and the possible causes behind them (8–12). In the British Regional Heart Study, data collected at the end of the 1970s revealed major differences in life-style factors, especially smoking, between social classes, as defined on the basis of occupation (10). The authors therefore concluded that the social class differences in CHD risk were mainly explained by life-style factors, in the first place by smoking. However, during the 1980s occupational class differences in life-style factors have considerably decreased, at least in the Nordic countries, while the differences in CHD risks have persisted (13).

Using data collected in the Helsinki Heart Study, we attempted to evaluate the CHD risk associated with shift work and to explore its possible pathways in a population employed in industry. We especially studied the differences in CHD risks among white-collar day workers, blue-collar day workers, and blue-collar shift workers in order to evaluate the role of shift work in the occupational class gradient of CHD risk.

Subjects and methods

Study population

The subjects were selected from participants of the first screening visit for the Helsinki Heart Study, a 5-year, placebo-controlled coronary prevention trial of middle-aged men (40–55 years at entry) (14–15). The participants for the trial were selected via 2 successive screenings from 2 government agencies and 5 industrial companies. The industrial cohort comprised men working in oil refinery plants, the forestry industry (paper, sawmill, plywood), and heavy engineering.

The volunteers were eligible for the study if their serum nonhigh-density lipoprotein cholesterol was ≥ 5.2 mmol/l in both pretreatment screenings and if they had no evidence of CHD or any other major illness.

In the present follow-up cohort only the participants employed in industry were included. The subjects for the present study originated from different selection phases of the Helsinki Heart Study; this procedure was followed to ensure that the subjects were representative of the source population. First, a reference group was selected by systematic sampling from among the people who did not fulfill the selection criteria in the first screening (figure 1). Second, all those who did fulfill the criteria in the first screening, but not in the second, were chosen as a second reference group (the "chol group"). At the end of the double blind trial, a psychosocial questionnaire was mailed to those in the trial or in the chol or reference groups. The response rate of the industrial group was 70%. Of the 1947 workers who responded, we excluded 127 subjects with missing information on occupation or shift-work status, and additionally a small group of 14 subjects who worked part-time were excluded.

Occupation and shift work status

Broad occupational categories were used in the present study, but the information was based on the 3-digit occupational code used in the 1980 census — a Finnish version of the Nordic Classification of Occupations from 1965. This information was obtained by record linkage from Statistics Finland. As the study group was identified at the first screening visit in 1982, those who entered their job between 1980 and 1982 could have occupational codes that were not industrial ones. In part of the analyses these newly employed persons were treated separately. In most of the analyses occupation was used as a dichotomized variable: white-collar workers (academic and clerical) versus blue-collar industrial workers. The latter group comprised the occupational categories iron and metal ware work, machine work in plants, wood work, and chemical process work.

Shift work was recorded in the questionnaire on the following 6-point scale: 1 = day work, 2 = part-time

Figure 1. Numbers of industry-employed participants in different phases of the Helsinki Heart Study. After the double blind trial the treatment group was revealed to the participants, and they could choose whether or not to continue with the medication. (GG = gemfibrozil during the double blind trial and continued on gemfibrozil, PG = placebo during the double blind trial and on gemfibrozil during open-label follow-up, GN and PN = gemfibrozil or placebo during the double blind, but not on gemfibrozil during the open-label trial, chol = reference group that fulfilled the criteria in the first screening but not in the second)

work, 3 = 2-shift work, 4 = 3-shift work, 5 = irregular work and 6 = night work. In the analyses a dichotomized variable was used (1 = day work, 2 = shift work, all combined), but also a 3-point scale was used (1 = day work, 2 = 2-shift work, 3 = 3-shift work) including irregular and night workers. Part of the 2-shift workers occasionally worked in 3 shifts. The aforementioned 4 occupational categories were all found in every shift-work group, although in different proportions. Almost half of the 3-shift workers were involved in chemical processing, while wood workers were the most frequently found among 2-shift workers. The shift schedules of the individual plants differed slightly. However, most of the sites had a continuous shift system (5 teams with a shift cycle of 20 days), working 4 morning, 4 evening, and 4 night shifts in a row, with 1 free day between successive shifts and 5 free days after the last episode of shifts. The direction or order of the shifts varied between the sites. In addition, a rapidly rotating continuous shift system (2 morning, 2 evening and 2 night shifts with 4 free days at the end, the shift cycle being 10 days) was used in a minority of the plants.

In this industrial study population 71% of the participants were blue-collar workers, and 37% of the total population were shift workers, either in 2- or 3-shift work (table 1). Among the blue-collar workers 48% were shift workers compared with only 9% among the white-collar workers. Most of the participants in the shift work groups had held their jobs for more than 5 years; of the 3-shift workers, 68% had held their present job for more than 20 years.

Life-style factors, blood pressure and serum lipids

All the background factors used in the present study were recorded at the first screening visit in 1982. In the

interview smoking habits were recorded on a 7-point scale, taking into account the number of cigarettes smoked and the time at which the respondent had given up smoking. In the present study a dichotomized variable was used, 0 for never or past smoking and 1 for current smoking. For recording alcohol consumption, a modified questionnaire of the Scandinavian drinking survey (16) was used. The reported quantities and the number of drinking occasions were converted into amounts of absolute alcohol (centiliters per year). In some analyses a dichotomized variable was used with a cutoff point of 250 cl/year. Leisure-time physical activity was recorded with the 4-point Gothenburg scale (17), but a dichotomized variable was also used. Body mass index was calculated as weight in kilograms divided by the square of the height in meters. Blood pressure was recorded from the right arm at the first screening visit with calibrated mercury sphygmomanometers with cuffs measuring 12 × 40 cm. The measurement was carried out in a sitting position before the blood sample was taken. The lipid measurements in this lipid modulation trial have been described in detail elsewhere (14, 15).

Job stressors

The job stress questionnaire was that proposed by Karasek (18) and further developed by Theorell et al (19), with 11 questions to be answered on a 4-point scale. (See the appendix.) The responses were used to form 2 sum scales, decision latitude and psychological demands, as proposed by Karasek.

Assessment of end points and the follow-up

The psychosocial questionnaire was mailed to the study population at the end of the double blind trial in 1986–1987. Those who had participated in the trial were then

Table 1. Level of some background factors by groups formed on the basis of crude occupational classification and shift-work status in the cohort of industry-employed responders to the psychosocial questionnaire in the Helsinki Heart Study.

Occupational group	N	Previous diagnosis of cardiovascular disease	Mean age (years)	Present shift work (%)		
				0–5 years	5–20 years	> 20 years
Academic and clerical						
Day work	477	7.1	52.3			
Shift work ^a	47	17.1	52.3	11.1	37.8	51.1
Industrial workers in plant or machine operation						
Day work	511	9.6	52.9			
Two-shift work	160	5.1	51.6	14.4	45.3	40.3
Three-shift work ^b	404	7.2	52.6	2.4	29.5	68.1
Other work in industry ^c						
Day work	152	7.0	53.4			
Shift work ^a	55	5.0	52.4	5.0	51.6	43.3

^a Various schedules.

^b Including 13 subjects with same jobs, but reporting irregular or night shift work.

^c Includes small special groups (guardians, transportation workers, etc) and those who reported jobs other than industrial ones in the 1980 census.

offered the opportunity to continue in an "open label" trial with biannual medical examinations and free treatment with gemfibrozil. Part of the former placebo subjects opted to continue with gemfibrozil, as did part of the former gemfibrozil subjects (figure 1).

Our follow-up lasted from the administration of the questionnaire to the end of 1993, with a mean follow-up time of 5.6 years. The end points were obtained from the Hospital Discharge Register and Register of Deaths kept by Statistics Finland. Several studies have found these registers accurate enough for epidemiologic purposes in studies of CHD (20, 21). In accordance with our previous study (21), our definition of CHD was based on codes 410–414 of the International Classification of Diseases, 9th revision.

Among the blue-collar workers, the shift workers had a lower prevalence of previous hospitalizations due to any form of cardiovascular diseases than the day workers, but among the academic and clerical workers the small shift work group had a 2.4 times greater prevalence than the day workers (table 1).

Statistical methods

We compared the relative risks of CHD associated with shift work in different subgroups of industrial workers to evaluate the stability of the estimate across different worker groups, but also to evaluate the effect of other intervening factors. The effect of the CHD risk factors presumably involved in the shift work—CHD pathway was estimated by adding them one by one to the risk model. To take into account loss of follow-up due to factors other than CHD end points, all the relative risks were estimated using Cox proportional hazards models (22).

Figure 2. Crude incidences of coronary heart disease (CHD) among the industry-employed men by shift work status and occupational category. [Closed bars = all workers included, open bars = those with previously (prev.) diagnosed cardiovascular disease (cvd) excluded]

Results

Occupation, shift work and risk of coronary heart disease

We compared the crude incidences of CHD in different groups formed on the basis of occupation and shift-work status, and, as a previous diagnosis of some form of cardiovascular disease implies an increased risk of CHD during follow-up, we explored the effect of excluding the subjects with a previous cardiovascular disease diagnosis (figure 2). A risk peak was found among shift working academic and clerical men, but this risk nevertheless disappeared when those with a previous cardiovascular disease diagnosis were omitted from the analysis. An opposite trend was seen in the third group of workers, while, for permanently working blue-collar men, the estimate of the relative risk due to shift work remained approximately the same, whether or not those with a previous diagnosis of cardiovascular disease were omitted.

When both industrial groups were combined and compared with the academic and office groups, their relative risk (RR) was 1.40 ($P = 0.05$) when age was allowed for in the model. If all the shift workers were compared with the day workers, they had a relative risk of 1.52 ($p = 0.01$) when age was allowed for, and 1.38 ($P \leq 0.05$) when systolic blood pressure, serum total cholesterol, and the life-style factors were also allowed for in the model (table 2). As a substantial part of the study population (31%) was receiving treatment with gemfibrozil during the follow-up, we also checked whether exclusion of those under treatment would change the risk pattern. Interestingly, it was found that gemfibrozil had substantially flattened the risk pattern (ie, its effect was greater on shift workers than on day workers). When all the material available was used, we thus somewhat underestimated the risk of CHD due to shift work.

Coronary heart disease risk in association with two-shift and three-shift work

When studying the CHD risk associated with different forms of industrial shift work, we focused largely, and as far as possible, on occupationally homogeneous groups (table 3). The 2-shift machine or plant workers had a 51% excess risk (not significant) when compared with corresponding day workers and an 89% excess ($P < 0.04$) when compared with the white-collar day workers. The corresponding figures for the 3-shift workers were 34% (not significant) and 69% ($P < 0.03$). If those with previously diagnosed cardiovascular disease were excluded, no excess risk remained in association with blue-collar day work when compared with white-collar day work — all excess risk was found among the blue-collar shift workers.

Table 2. Relative risks (RR) for coronary heart disease among shift workers compared with corresponding day workers in different industry-employed subgroups. (95% CI = 95% confidence interval, CVD = cardiovascular disease)

Risk group	Reference group	No exclusions				Those on gemfibrozil or with previously diagnosed CVD excluded			
		Age		Age and smoking, total cholesterol, systolic blood pressure, body mass index, spare time physical activity and alcohol consumption		Age		Age and smoking, total cholesterol, systolic blood pressure, body mass index, spare time physical activity and alcohol consumption	
		RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
All shift workers	All day workers	1.52	1.11—2.07	1.38	1.01—1.89	1.70	0.92—3.14	1.50	0.80—2.81
All blue-collar shift workers	All blue-collar day workers	1.35	0.94—1.93	1.30	0.91—1.87	1.73	0.84—3.57	1.61	0.77—3.33
Permanent shift workers in plant or machine operation	Permanent day workers in plant or machine operation	1.39	0.94—2.08	1.33	0.89—1.99	1.75	0.78—3.92	1.59	0.70—3.61

Table 3. Relative risks (RR)^a for coronary heart disease in industry-working subgroups of the Helsinki Heart Study cohort by crude classification of occupation and shift work status. (95% CI = 95% confidence interval, CVD = cardiovascular disease)

Occupational group	Model ^a					
	No exclusions		Those with previously diagnosed CVD excluded		Those on gemfibrozil or with previously diagnosed CVD excluded	
	RR	95% CI	RR	95% CI	RR	95% CI
Academic and clerical workers						
Day work	1	.	1	.	1	.
Industrial workers in plant or machine operation						
Day work	1.3	0.8—2.0	1.2	0.7—2.1	1.0	0.4—2.5
Two-shift work	1.9	1.1—3.4	1.9	0.98—3.5	2.1	0.8—5.4
Three-shift work	1.7	1.1—2.7	1.6	0.94—2.7	1.5	0.5—4.3

^a The relative risks were derived via Cox regression models with age as a covariate.

Table 4. Occupation, shift work status, and prevalence of some life-style factors measured at the beginning of the Helsinki Heart Study trial. (NS = not significant)

Occupational group	N	Smokers (%)	Moderate or heavy consumption of alcohol (%)	Body mass index, ≥ 30 kg/m ² (%)	Physically active during spare time (%)
Academic and clerical workers					
Day work	477	28.2	60.6	9.7	41.2
Industrial workers in plant or machine operation					
Day work	511	32.5	54.0	10.2	36.3
Two-shift work	160	33.1	53.8	8.1	39.7
Three-shift work	404	34.2	49.8	13.4	39.6
Total	1552	31.7	54.9	10.6	39.0
Statistical significance of difference (chi square test)		NS	P = 0.07	NS	NS

Possible pathways for the effect of shift work on coronary heart disease risk

The 3-shift workers had the highest percentage of smokers and people severely overweight (table 4). They also

had the lowest proportion of alcohol consumers. Interestingly, all the shift workers engaged in vigorous physical activity during their spare time almost to the same extent as the white-collar day working men. The systolic blood

Table 5. Mean levels of systolic blood pressure, total cholesterol and high-density lipoprotein (HDL) cholesterol at the beginning of the Helsinki Heart Study^a by occupational category and shift-work status.

Occupational group	Systolic blood pressure (mm Hg)		Total cholesterol		HDL cholesterol	
	Mean	SD	Mean	SD	Mean	SD
Academic and clerical workers						
Day work	137	16	6.8	1.1	1.24	0.29
Industrial workers in plant or machine operation						
Day work	141	16	6.9	1.1	1.25	0.30
Two-shift work	142	16	6.9	1.1	1.26	0.29
Three-shift work	142	17	6.8	1.1	1.24	0.30
ANOVA test for equality of means	P = 0.000		NS		NS	

^a The measurements were made before any treatment or health education of the subjects and thus 4–5 years before the interview.

Table 6. Distribution of subjects (%) by quartiles of job-decision latitude and psychological demands in groups formed on the basis of crude occupational classification and shift-work status.

Occupational group	Job decision latitude						Psychological demands					
	N	Quartile				Total	N	Quartile				Total
		I	II	III	IV			I	II	III	IV	
Academic and clerical workers												
Day work	473	5.5	16.5	41.0	37.0	100	475	19.4	25.3	24.6	30.7	100
Industrial workers in plant or machine operation												
Day work	502	18.7	28.5	31.3	21.5	100	506	33.0	22.5	22.3	22.1	100
Two-shift work	157	40.8	20.4	26.8	12.1	100	158	20.3	27.8	22.8	29.1	100
Three-shift work	396	43.2	27.8	21.7	7.3	100	398	34.9	27.6	19.6	17.8	100
Total	1528	23.2	23.8	31.3	21.7	100	1537	28.0	25.2	22.4	24.4	100
Statistical significance of difference (chi-square test)		P = 0.000						P = 0.000				

pressure differed significantly between the different groups, the lowest level occurring among the day working academic and clerical employees and the highest level occurring among the blue-collar shift workers (table 5). There were no differences in the levels of total cholesterol or high-density lipoprotein cholesterol in the groups considered.

The scores for both components of the Karasek job-strain indicator, job-decision latitude and the psychological demands, differed substantially between the groups (table 6). Academic and clerical day workers reported high levels of job-decision latitude, 78% reporting scores above the median. In contrast 71% of the 3-shift workers reported scores below the median and 43% had scores in the lowest quartile. The 3-shift workers also reported low scores psychological demands.

To examine further the pathways of the effect of shift work on the risk of CHD, we repeated the risk analysis using different CHD risk factors as covariates (table 7). The addition of systolic blood pressure or smoking to the model decreased the risk due to shift work, but also the risk involved in blue-collar day work. All these groups had higher levels of these risk factors than the white-

collar day workers did. When alcohol consumption, a possible protective factor for CHD, was added to the model, the CHD risk among the blue-collar workers was accentuated. The components of job strain explained part of the blue-collar CHD risk, especially that among the 3-shift workers. All the life-style risk factors that were found to be more prevalent among shift workers thus explained some part of the CHD risk, but a substantial part still remained unexplained.

Discussion

Our study focused on CHD risk due to long-term shift work among permanently working men in their late middle age. After identification of the cohort, all of its members were followed regardless of whether they changed jobs or retired. Since the selection of well-tolerating shift workers had probably already taken place (23), early dropouts did not occur in this study. It is likely that part of them were in the day working groups in corresponding occupations (ie, in the reference group). Nevertheless

Table 7. Effect of different covariates on the relative risk (RR)^a of coronary heart disease in industry-employed subgroups of the Helsinki Heart Study. (95% CI = 95% confidence interval)

Occupational group	Covariates in the model ^a							
	Age and systolic blood pressure		Age and alcohol consumption		Age, alcohol consumption, smoking and leisure-time physical activity		Age and the components of job strain ^b	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Academic and clerical workers								
Day work	1	.	1	.	1	.	1	.
Industrial workers in plant or machine operation								
Day work	1.2	0.8–1.9	1.3	0.8–2.0	1.2	0.8–2.0	1.2	0.7–2.0
Two-shift work	1.7	0.96–3.1	2.0	1.1–3.6	1.9	1.0–3.3	1.8	0.95–3.3
Three-shift work	1.6	0.98–2.5	1.7	1.1–2.8	1.7	1.0–2.7	1.6	0.9–2.6

^a The relative risks were derived via Cox regression models.

^b Dimensions job-decision latitude and psychological demands.

a clear excess risk was found for the shift workers during the 6-year follow-up.

To estimate the CHD risk due to shift work, we performed several analyses in different subgroups and with different covariates. Whatever the framework for the analyses, some general trends emerged. First, the shift workers had an excess risk of 30–50% with some variation by subgroup. Second, the excess risk of CHD among the blue-collar workers, when compared with the white-collar workers, was mainly found among the blue-collar shift workers.

In their follow-up of 504 blue-collar paper mill workers, Knutsson et al (4) found a 40% excess risk among shift workers when compared with day workers in corresponding occupations. Their subjects were younger at entry than in our study, but the follow-up time was 15 years against our 6 years. Therefore both studies partially covered the same period of employment phase. Our 3-shift workers were mainly paper mill workers, and their relative risk compared with that of day workers was similar to that reported by Knutsson and his colleagues. In addition, our results show that, even in other branches of industry, shift work is associated with a similar (30–50%) excess risk of CHD. In contrast to the study of Knutsson et al (4), we saw only a weak dose-response pattern with increasing (measured in years) exposure to shift work, possibly because our sample had a higher proportion of men with a shift-work experience of over 20 years already at entry into the study. It is possible that the peculiar finding of a lower CHD risk among 3-shift workers than among the 2-shift workers can be at least partially explained by the reduced risk among the shift workers with over 20 years of employment, as described by Knutsson et al. Occupational differences in physical work load may also contribute to the higher CHD risk among the 2-shift workers, as they were mainly working in the plywood, sawmill and metal industries, while the

3-shift workers were mostly working in paper or oil refining industries.

Several putative pathways have been suggested to explain the association of shift work with CHD. According to a much-cited model by Knutsson (24), the effect could take place via (i) mismatch of circadian rhythms, (ii) behavioral changes (direct), or (iii) disturbed socio-temporal patterns. All these paths could partially operate via changes in life-style factors. We studied the impact of several life-style factors and found differences in alcohol consumption, smoking, and body mass index. However, all these differences were minor and could not explain the shift-work effect on CHD either when they were considered individually or in combination. The major differences in the smoking prevalences between the shift and day workers (24 percentage points) in the 1968 recording by Knutsson et al (4) are not equaled by our less than 2 percentage points in 1982. Pocock et al (10) also reported major differences in the prevalences of smoking and leisure-time physical activity between occupational groups. In our study both differences were less than 6 percentage points. In this instance we have assumed that the life-style factors partly mediate the effect of shift work on CHD, but it could be argued that they are pure confounders of the effect. In any case, regardless of whether we view the life-style factors as intermediate steps in the pathway leading from shift work to CHD or whether we view them as mere confounders, a substantial part of the CHD risk associated with shift work remained after adjustment for these factors.

Our results suggest that, in addition to the life-style pathway, the shift work effect may pass directly through a stress pathway. First, the mismatch of circadian rhythms with accompanying sleep disturbances is a source of long-term stress (25). Second, shift workers have reported low scores on job-decision latitude, nearly half of them scoring below the first quartile. Three-shift

workers also reported low job demands. A monotonous job with low demands and limited influence is a well-established source of stress (5, 18). The finding of significant differences in systolic blood pressure between the groups would also be consistent with the stress pathway, although other pathways could certainly also lead to these differences.

There is increasing evidence that long-term stress affects the blood coagulation system (26), thus intervening in thrombus formation. Recently Räikkönen et al (27) showed that chronic stress, defined as feelings of fatigue, lack of energy, increased irritability, and demoralization, was positively associated with plasminogen activator inhibitor-1 (PAI-1) antigen (27), while deficient fibrinolysis, due to an increase in PAI-1, may be involved in thrombosis (28). Approximately 31% of the subjects in our study were receiving the drug gemfibrozil, a fibrate derivative designed for CHD prevention by modulation of serum lipid levels. Meanwhile, it was discovered that gemfibrozil may also enhance fibrinolysis by direct diminution of endogenous PAI-1 synthesis (29) and thus prevent thrombus formation and myocardial infarction. Although no hemostatic parameters were measured in the Helsinki Heart Study, the results from our previous study (30) still indirectly lend some support to the hypothesis that an effect on the fibrinolytic system was one pathway in the effect of gemfibrozil in CHD prevention. Table 2 shows clearly that gemfibrozil had a stronger preventive effect on shift workers than on the reference group with white-collar day workers. The effect could not operate via the modulation of levels of total cholesterol or HDL cholesterol, as there were no base-line differences in these levels, but it could certainly utilize the PAI-1 levels if our stress hypothesis is valid. The stress pathway and the life-style factor pathway may also be closely related, as smoking, hypertension, and high body mass index are often related to long-term stress and attempts to cope with it (31).

The estimate given for the effect of shift work is probably too low, for several reasons. First, the treatment with gemfibrozil flattened the risk pattern as seen in table 2. Second, part of the people who dropped out before the beginning of the follow-up were probably from the reference group of day workers, and, if so, their risk would be increased and the relative risk of shift work would be lowered. Third, the estimated risks were mainly long-term effects on people who were well adapted to shift work. When those with a previous diagnosis of cardiovascular disease are excluded, we can exclude part of the effects of a long-term exposure to shift work, and our estimate represents the effect among "truly well-adapted" workers.

In conclusion, shift workers had an excess risk of coronary heart disease of 30–50% in comparison with day workers. Shift work was found to be an important

part of the occupational gradient in CHD risk among industrial workers. There were some differences in life-style factors such as alcohol consumption, smoking, and body mass index, and highly significant differences in levels of systolic blood pressure, but these differences were not sufficient to explain the excess CHD risk among the shift workers. Some evidence was found for the hypothesis that a direct, stress-related pathway possibly originating from disturbances in circadian rhythms or from job stressors could be at work, and the effect may operate via impaired fibrinolysis rather than through the modification of lipid levels.

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Appendix

Items in the job stress questionnaire

- Q1. Does your job require that you work very fast?
- Q2. Does your job require that you work very hard?
- Q3. Are you asked to do an excessive amount of work?
- Q4. Do you have enough time to get the job done?
- Q5. Are you exposed to conflicting demands on your job?
- Q6. Do you learn new things in your job?
- Q7. Does your job require a high level of skill?
- Q8. Does your job require creativity?
- Q9. Do you have to do things over and over on your job?

- Q10. Do you have freedom to decide how you do your job?
- Q11. Do you have freedom to decide what is done on your job?

The scores for job-decision latitude and psychological demands were calculated as weighted sums (18, 32):

$$\begin{aligned} \text{job-decision latitude} &= Q6+Q7+Q8+(5-Q9)+27 \cdot (Q10+Q11) \\ \text{psychological demands} &= 3 \cdot (Q1+Q2)+2 \cdot (Q3+Q5+(5-Q4)) \end{aligned}$$

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