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Scientific Symposium
The Health Effects of Shift Work
Toronto, April 12, 2010

SUMMARY REPORT

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IMPORTANT NOTE

This document is a summary of the proceedings of a symposium. The statements and observations contained in this summary do not constitute formal recommendations by the Occupational Cancer Research Centre or the Institute for Work & Health concerning the evidence regarding shift work and health.

INTRODUCTION

On April 12, 2010, more than 100 researchers and representatives from the employer, labour and workers' compensation communities — primarily from Ontario, but also other parts of Canada, the United States and Europe — came together in Toronto to explore the health effects of shift work. Co-hosted by the Occupational Cancer Research Centre and the Institute for Work & Health, the invitation-only event aimed to:

- provide an overview from leading scientific experts on research evidence about the health effects of shift work, and
- solicit from presenters and participants the key gaps in the research evidence on the health effects of shift work.

ABOUT THE CO-HOSTS

The Occupational Cancer Research Centre (OCRC) is the first of its kind in Canada, and was created to bridge the gaps in our knowledge of occupation-related cancers and to translate these findings into preventive programs to control workplace exposures and improve the health of Ontarians. Our vision is the prevention of occupational cancer through the identification and elimination of exposures to carcinogens in the workplace - towards a cancer free workplace. This major new initiative is a unique partnership that unites research, healthcare, workplace safety, labour and industry groups. It is jointly funded by Cancer Care Ontario, the Workplace Safety and Insurance Board and the Canadian Cancer Society, Ontario Division and was developed in collaboration with the United Steelworkers Union.

The Institute for Work & Health (IWH) is an independent, not-for-profit research organization that aims to protect and improve the health of working people by providing useful, relevant research on the prevention of workplace injury, illness and disability. It conducts and shares research with policy-makers, workers and workplaces, clinicians and health and safety professionals. IWH operates with support from the Workplace Safety and Insurance Board of Ontario.

KEY MESSAGES ARISING FROM SYMPOSIUM

A. Key findings presented at the symposium

- Shift work is common. About one-quarter of the workforce in North America and Europe is engaged in shift work requiring working at night. In Canada, 11 per cent of workers work rotating shifts, six per cent work regular evening shifts and two per cent work regular night shifts.
- Shift work can result in sleep disruption and sleep deprivation, and in sleepiness/fatigue at work.
- Night shift work has been associated with an increase in breast cancer in women who work rotating shifts for longer durations (i.e. 30-plus years).
- A number of biological mechanisms to explain the association between light at night and cancer risk are being explored. The key ones are the suppression of the normal night-time production of melatonin and the disruption of the circadian gene function.
- Evidence from animal studies supports the link between circadian disruption (in the form of suppressed melatonin production) and the growth of tumours.
- In 2007, based on limited evidence from human studies and sufficient evidence from animal experiments, the International Agency for Research on Cancer (IARC) classified “shift work that involves circadian disruption” (i.e. night shift work) as a probable human carcinogen (Group 2A).
- There is strong evidence that night, evening, rotating and irregular shifts are associated with an elevated risk of workplace injuries.
- There is not enough high quality evidence to reach firm conclusions on the influence of shift work on heart disease.
- There is evidence that shift work has a moderate negative effect on fetal growth in pregnant women.

B. Key gaps in the research

- The epidemiological and animal evidence indicate links between shift work and some poor health outcomes. Additional information is needed to resolve inconsistencies and improve strength of information regarding:
 - the magnitude of the risk relative to specific health outcomes,
 - how, exactly, shift work causes poor health outcomes in humans, and
 - which shift workers, in particular, may be more susceptible or resistant to risk, because of individual susceptibility factors, sleep patterns, the nature and duration of their shift work, and working conditions such as light levels.
- Shift work is a complex phenomenon and researchers need to develop and use common definitions of “shift work” and shift work exposure measures in order to increase the power, generalizability and replicability of study findings.
- Measurement and characterization of shift work in epidemiological studies is challenging. More detailed information should be collected on exposure factors such as:
 - the length of shift worked (e.g. start and stop time),
 - number of days on shift (e.g. pattern of shift work),
 - number of years working shifts, and
 - the quality/intensity/duration/timing of light on a shift.
- To the extent possible, current sources of information, such as cancer databases, workers’ compensation data and payroll records, should be used to collect information on shift work and health outcomes.
- More information is needed on the biologic mechanisms through which shift work acts on various ill-health outcomes, such as melatonin levels, genetic predisposition to circadian disruption, sleep disruption, impact on the immune system, and the effects/role of vitamin D.
- Research on shift work and cancer should expand beyond breast cancer in women to include other types of cancer and men.

REPORT ON SYMPOSIUM PROCEEDINGS

The symposium was organized in four parts. Each of the first three parts included three presentations from leading researchers on the health effects of shift work and was followed by a discussion. The fourth segment was an open discussion with all presenters and participants on the research gaps identified in the day's proceedings and suggested future priorities.

The discussions were moderated by Kristan Aronson. Dr. Aronson is a professor and research epidemiologist in the Division of Cancer Care and Epidemiology, Cancer Research Institute, Queen's University, Kingston, Ontario, Canada.

What follows is a summary of the presentations and discussions in each of the four parts of the symposium. This includes an overview of each of the research presentations, as well as a list of the research priorities identified by the speaker during his or her presentation and comments and questions from participants during the post-presentation discussions. It concludes with a summary of research issues addressed during the wrap-up discussion.

Part I: Prevalence, key trends and biological mechanisms

The prevalence of shift work in Canada

Paul Demers, School of Occupational and Environmental Hygiene, University of British Columbia (and newly-named Director of OCRC)

Shift work is common among Canada's working population. Based on the 2006 Survey of Labour and Income Dynamics (SLID) conducted by Statistics Canada, about 11 per cent of employed Canadians work rotating shifts, while six per cent work regular evenings and two per cent work regular night shifts. The prevalence of both rotating and evening work is much higher among people under 30 than at older ages. The number of women working evening, night and, especially, rotating shifts has increased dramatically over the last 10 years.

The industrial sectors in Canada with the highest number of shift workers (over 350,000 each, accounting for over 20 per cent of their workforces) are trade, manufacturing, accommodation and food services, and health care and social assistance. The overall prevalence of shift work is similar for women and men. However, there are gender differences in shift work patterns by sector of employment. Many more women than men work in the health care sector, while many more men than women work in manufacturing.

Knowing the employment patterns of shift work is important because they tell us where we should target research, surveillance, and prevention and mediation efforts. Our understanding of the changing patterns of shift work, however, is still incomplete.

Research priorities

- Increase the number of people surveyed in population studies to provide a better understanding of the prevalence of shift work. Although the SLID sample is large at about 30,000, women on the night shift make up only one per cent of the sample.
- Future population surveys on shift work should include start and stop times to provide more detail about the patterns of shift work.
- Conduct life-time surveys (e.g. over a span of 30 years).

Shift work and sleep disturbance

Torbjörn Åkerstedt, Stress Research Institute, Stockholm University

Available studies indicate that sleep after a night shift or before an early morning shift is temporarily reduced, in most workers, by one to three hours, resulting in only five to seven hours of sleep. However, sleeping patterns after the night shift vary widely, and about 15 per cent of night shift workers get three hours of sleep or less. Workers on evening shifts do not appear, on average, to suffer sleep loss.

With increased sleep on days off, it appears that most night shift workers do not suffer chronic sleep loss over time. The main sleep problem among shift workers may be sleepiness and fatigue during work hours. Sleepiness among shift workers is due in part to being awake for an extended period of time and to working during the “low” period of the circadian rhythm.

Sleepiness appears to be much greater on the night shift and, to a lesser extent, on the morning shift. It also appears that individual vulnerability to shift work is mainly linked to sleepiness. Considerable research supports the assumption that the sleepiness associated with night work is linked to performance errors and accidents.

Research priorities:

- Determine if there is a subgroup of workers especially susceptible to chronic sleep deficit and, if so, what its characteristics are.
- Determine the cause of the sleep deficit. Is it related to circadian disruption, low melatonin, or immune dysregulation?
- Explore the relationship between chronic sleep deficit and shift work tolerance.
- Conduct studies of “good” and “bad” shift schedules that define parameters such as time of day of the shift, speed of the shift rotation, direction of the shift rotation on sleepiness and health outcomes.
- Conduct longitudinal studies that follow individuals before, during and after shift work.

Shift work and breast cancer – the need for mechanisms

Richard Stevens, Department of Community Medicine and Health Care, University of Connecticut

Mounting evidence supports the hypothesis that non-day shift work increases the risk of breast cancer in women. In 2007, based on limited human studies and sufficient animal experiments, the International Agency for Research on Cancer (IARC) classified “shift work that involves circadian disruption” as a probable human carcinogen (Group 2A).

It is imperative to understand the mechanisms by which shift work may increase the risk of cancer in humans in order to design prevention and mitigation strategies. The two mechanisms gaining prominence are both linked to exposure to light at night: (1) the suppression of melatonin, and (2) the disruption of the circadian gene function. These are not mutually exclusive and evidence exists for each from both human and laboratory research.

Research priorities:

- Continue to investigate the impact of light on the circadian system in humans and the cancer risk it poses, and replicate the findings of studies already conducted.
- Learn more about the biophysics of phototransduction at the retina, the molecular genetics of circadian clocks, the endocrine aspects of circadian physiology, and the epidemiology of breast cancer in women who work shifts.

Research gaps identified during Part I discussion

- Need studies focused on various aspects of shift work and possible carcinogenic mechanisms. Determine what aspect of shift work drives these effects. Is it the shift schedule? The quality of light?
- Need to know more about workers' choice regarding shift work. Do they choose it (as young people may do to optimize their free time while earning a good wage), or do they have no choice? Is it driven by employers and the needs of the 24-hour global economy? The impact of socioeconomic factors (manager versus labourer, income bracket, etc.) needs to be evaluated.
- Need more studies on clock-controlled genes – 10 per cent of genes are clock-controlled – and whether the mechanism at work may play a role in cancers beyond breast cancer in women.
- Need to use a larger window in population studies in order to truly show trends in the prevalence of shift work in Canada.

Part II: Night work, cancer and other possible health effects

Shift work and adverse health effects – possible biological mechanisms

Scott Davis, School of Public Health, University of Washington

A number of biological mechanisms have been proposed to explain the association between night shift work and breast cancer in women and to a lesser extent, prostate cancer in men.

Suppression of the night-time production of melatonin due to exposure to light at night has been the major focus. Research has shown that melatonin (or the lack of melatonin) may act indirectly or directly in causing cancer.

Indirect effects occur because decreased melatonin can increase the release of gonadotropins from the pituitary and estrogen from the ovaries, thereby affecting the growth of hormone-dependent tumours (such as breast cancer). Studies also show that melatonin has a direct beneficial effect in inhibiting the development and/or growth of tumours in a variety of ways.

Other potential biological mechanisms possibly involved include the role of vitamin D in reducing cancer risk and the role of genetics (namely, clock-controlled genes) in adapting to circadian disruption.

Research priorities:

- Determine exactly what aspects of night shift work are causing the increase in cancer risk. Is it light exposure, sleep disturbance, stress, or a combination of these and other factors? Designing epidemiological studies that can sort out these factors will require creative thinking.
- Evaluate the association between exposure to light at night and the risk of not only breast cancer, but also other cancers, including cancer risks among men.
- Conduct research that addresses individual susceptibility in order to tailor prevention efforts. Are some subgroups particularly susceptible? How do we identify them?
- Learn more about the biological basis for the detrimental effects of night shift work in order to design preventive interventions to reduce relevant exposures.

Night work, night light and cancer – animal evidence

David Blask, Laboratory of Chrono-Neuroendocrine Oncology, School of Medicine, Tulane University

Emerging data suggests night shift workers, particularly those on a rotating schedule, are at a significantly increased risk of developing breast cancer. It has been proposed that exposure to light at night among shift workers suppresses the nocturnal production of melatonin, which is responsible for telling all cells, including cancer cells, to go to sleep.

Because it is difficult for epidemiological studies to uncover causal links between light at night and the risk of breast cancer, and because testing the hypothesis through an experimental design among humans would be unethical, animal studies provide critical empirical evidence on the issue. Evidence from these animal studies appears to be sufficiently strong to support the link between circadian disruption (in the form of suppressed melatonin production) and the development and growth of tumours.

For example, among laboratory animals exposed to constant light or light at night (including dim light), melatonin production is virtually completely suppressed and tumours proliferate at a high rate. On the other hand, the growth of tumours is slowed among lab animals exposed to regular light/dark schedules or tumours infused with melatonin. The link between melatonin levels and cancer cell growth is very strong.

Research priorities

- Determine what aspects of light exposure at night (i.e. intensity spectrum, spatial pattern, duration and timing) result in the highest and lowest breast cancer risk in humans via circadian/melatonin disruption.
- Test the effects of light-exposure regimens that mimic the light exposure patterns actually experienced by shift workers at night on breast cancer development and growth in the experimental setting in animals. New strategies and tools should be evaluated so that we can better extrapolate between animals and humans.
- Examine the relative short- and long-term contributions of light-at-night-induced suppression of the nocturnal circadian melatonin signal versus circadian phase disruption to breast cancer initiation, growth, progression, invasion and metastasis.
- Determine the relationship and interaction between circadian melatonin signal strength, melatonin receptor expression sensitivity and dietary cancer-stimulatory/inhibitory factors in cancer-susceptible target tissues and risk for developing breast cancer in response to circadian disruption of melatonin by light at night.
- Examine the interactions between nocturnal circadian melatonin signal disruption by light at night and melatonin receptors, clock genes and cell proliferation/survival pathways that may be involved in regulating tumour development and/or tumour suppressor genes.

Light at night and health – the Nurses’ Health Study cohorts

Eva Schernhammer, Harvard Medical School, and Department of Epidemiology, Harvard School of Public Health

The Nurses’ Health Study (NHS) included two cohorts (1976, with a shift work question added in 1988, and 1989) for a total of 240,000 women followed for 30 years. The cohorts included a high prevalence of female night workers, which allowed researchers to study the health effects of exposure to light at night. Blood and urine samples were collected from about a third of the participants, which allowed researchers to study the association between melatonin levels and cancer.

Moderate increases in cancer risk were observed for women who had worked rotating shifts for longer durations. After controlling for major risk factors, job stress and socioeconomic status, shift work was found to significantly increase the risk of breast cancer (36 to 79 per cent increased relative risk), colon cancer (35 per cent elevated risk) and endometrial cancer (43 per cent elevated risk). In addition, higher melatonin levels were associated with lower breast cancer risk. Evidence from the NHS cohorts contributed to the IARC recommendation to classify night shift work as a probable carcinogen.

Regarding cardiovascular risk, the evidence implicating shift work in the NHS was less compelling. There was not enough evidence to associate cardiovascular risk with either melatonin levels or shift work.

Research priorities

- Standardize the definition of “shift work” in order to determine what aspects of shift schedules (such as shift length, frequency of rotation, number of hours worked per week) are the most detrimental to health.
- Search for new biologic markers other than melatonin for circadian disruption, such as chronotype (morningness versus eveningness) and sleep markers.
- Study the role of vitamin D.
- Study the impact of shift work on men (e.g. prostate cancer).
- Study gene-environment interactions – clock-controlled genes in particular – to see if we can identify subgroups of women who should stay away from night work.

Research gaps identified during Part II discussion

- Need research to determine the impact of the duration of shift work (e.g. the trend towards 12-hours shifts as opposed to eight-hour shifts, and the risk impact of the additional four hours).
- Expand research on the impact of different exposure situations and risk. For example, determine the impact of working three night shifts per week for 30-plus years versus working seven night shifts per week for a shorter duration.
- Explore the impact of different job classifications on the health effects of shift work, because different jobs bring different lighting conditions, stress levels, work organization, etc.
- Establish a uniform definition of “shift work.”
- Need more research on the effects of light exposure on cortisol levels.
- Need more research on melatonin supplements, including their long-term health effects.
- Need more consistency, strength of evidence and generalizability to confirm IARC’s classification of night shift work as a Group 2A “probable carcinogen,” to determine if this classification should be strengthened, and to support policies for compensating workers.
- Evaluate the relative contributions on intensity and duration of light at night on tumour growth.

Part III: Shift work and health effects

Shift work and the risk of work injury

Cameron Mustard, Institute for Work & Health, Toronto

There is strong evidence that night, evening, rotating and irregular shifts are associated with an elevated risk of occupational injury. According to population attributable risk calculations, six to seven per cent of workplace injuries can be attributed to shift work. These risks are generally understood to arise from two primary factors: (1) worker fatigue due to sleep disturbance, long work hours and their resulting effect on circadian rhythms, and (2) typically lower levels of supervision and co-worker support during non-daytime work schedules.

Nonetheless, shift work remains a relatively invisible hazard. This may be due to the fact that routine surveillance of injuries among shift workers is lacking. Surveillance information is needed to guide prevention efforts and inform the design of more sophisticated research to understand the specific mechanisms of hazards associated with non-regular work hours.

Potential approaches to monitoring work hours and work injury include the use of: (1) time-of-injury information on workers' compensation claims, (2) hospital emergency department records containing proxy information on time and cause of injury, and (3) labour market panel surveys that collect information on usual work schedules and incidents of work injury in the previous year.

Research priorities:

- Improve the quality of research on the health effects of shift work by collecting more information at the population level.
- Collect information on work hours (including time of day and duration), individual work demands and the availability of supervision over the 24-hour clock, as well as information on the health status and sleep patterns of workers who work regular and non-regular hours.
- Increase sample sizes of surveys to allow evaluation by industry.

Shift work and the risk of ischemic heart disease – a systematic review of the epidemiologic evidence
Poul Frost, Department of Occupational Medicine, Aarhus University Hospital, Denmark

Shift work may be related to heart disease because of the psychosocial, behavioural and/or physiological stresses caused by working non-standard work hours, although strong evidence on these mechanisms is missing. A systematic review published in 2009 synthesized high quality research findings on the relative risk of ischemic heart disease and night shift work.

Most studies looking at fatal heart attacks showed no, or weak, associations with shift work. Studies looking at both fatal and non-fatal heart attacks mostly showed modest positive associations with shift work. Our systematic review concluded that the available evidence on the influence of shift work on heart disease is insufficient at the present time.

The major limitation was that independent information on working hours at the individual level – e.g. hours worked, number of nights worked, years worked, light exposure levels was largely unavailable. This information is needed to assess risk relative to type of shift systems and cumulative exposures.

Research priorities

- Improve methods for assessing shift work in order to be able to evaluate risk relative to types of shift systems and cumulative exposures. Working hours at the individual level should form the basis for exposure assessment.
- Conduct a prospective follow-up study of men and women as they enter the labour market, collecting information on their working hours, social class, age and gender, and then tracking heart disease outcomes among those who work shifts and those who do not.

Shift work and pregnancy outcomes

Matteo Bonzini, Department of Experimental Medicine, University of Insubria, Italy

Non-traditional work schedules may be detrimental to pregnant women and their fetuses. Hormonal disturbances that result from sleep deprivation or circadian rhythm disruption, as well as increased stress as a result of work-life conflicts created by night shifts, could affect pregnancy outcomes.

An updated systematic review was conducted in 2010 to look at shift work exposure during pregnancy and the risk of preterm delivery, fetal growth retardation, and gestational hypertension and pre-eclampsia. The review found that shift work had a moderate negative effect on fetal growth (i.e. it was associated with being small for gestational age or low birth weight). No association was found for pre-term delivery (contrary to previous studies) and pre-eclampsia.

Given the link between shift work and fetal growth retardation, and despite the otherwise inconclusive nature of the review, women should be advised against working non-traditional work schedules during pregnancy and should always be allowed to change to daytime work.

Research priorities:

- Conduct pregnancy and birth outcome research that properly distinguishes between different types of shift work (e.g. rotating versus fixed shifts) because they may differently affect maternal hormonal balance and sleep behaviours.
- Conduct more high quality, larger studies on the effects of shift work on pre-term delivery and other pregnancy outcomes.

Research gaps identified during Part III discussion

- Exploit existing data repositories to measure and review health outcomes among shift workers (e.g. employer payroll information, cancer data banks, other public health registries).
- Measure the effect of circadian rhythm disruption resulting from shift work on myocardial infarctions.

Part IV: Open discussion on gaps in knowledge and priorities for future research

Dr. Kristan Aronson, the moderator for this session, commented that shift work has re-energized the field of occupational epidemiology. Much of the early work on the effects of shift work and health focused on injuries, accidents and cardiovascular disease. Research linking shift work with breast cancer and the subsequent IARC classification of night shift work as a probable carcinogen has stimulated further research into the health effects of shift work.

The moderator noted that, from animal studies to epidemiological evidence, there is agreement that, biologically, shift work has an effect on health. Although information is emerging, the specific mechanisms and pathways through which shift work acts remain largely unknown. Research to clarify and identify new mechanisms need to be undertaken as quickly as possible.

Key comments and questions raised in the discussion were as follows.

- The fundamental question that remains to be answered is how important is shift work relative to health? With the cohorts established we may be able in 10 or 15 years to have a clearer indication. One approach recommended was to ask the simple question: Have you ever done shift work – yes or no – and to use this to assess health risks. However, many participants in the symposium called for more detailed questions in shift work studies and population surveys. They felt that knowing more information about shift patterns – e.g. about the length of shift worked (start and stop times), number of days on shift, type of shift (permanent versus rotating), the nature (forwards versus backwards) and speed of rotating shifts, number of years working shifts, the quality and intensity of light on a shift – will provide stronger answers about those at risk and better direction regarding where to focus research, prevention and mediation efforts.
- Better exposure information is needed to determine who specifically is at risk in order to address the questions of people concerned about shift work and health, especially cancer. We need to develop a common approach to exposure assessment in epidemiological studies in order to determine which shift workers are more specifically at risk.
- We need to continue to explore the biological mechanisms behind the effects of shift work on health.
- Although researchers have begun discussing common definitions of shift work and exposure assessments, the exercise is challenging. That is due, in part, to the differing study rationales, which are targeted to funders' priorities.
- More specific information on shift work and poor health/work injuries may already be available through existing sources and needs to be made available to researchers. Workers' logs or work diaries may be a way to collect detailed information. The web might prove a useful tool for collecting worker information.
- One strategy that may be readily within our reach would be to conduct more intermediate studies that look at, for example, the effects of exposure to light at night on intermediate pathways (e.g. melatonin) instead of disease outcomes. This kind of focus would be of great

value by providing fairly quick knowledge about individual factors. Some researchers are already starting to take this approach.

- In conducting intermediate studies, all mechanisms that may contribute to poor health outcomes among shift workers, from psychosocial factors to circadian rhythms, should initially be addressed, and all outcomes (e.g. obesity), not just biomarkers, should be included.
- It would be helpful to have several large studies to confirm the relative risk of shift work to health outcomes such as breast and other cancers.
- Socioeconomic factors should be included in epidemiological studies of shift work and health outcomes.
- Researchers should have more direct interactions with shift workers and labour representatives in order to make the research deeper and more empowering of those affected. In a similar vein, it is important to include employers because they have control over working conditions.
- Interventions designed to prevent or mitigate negative health effects of shift work should be studied and considered, even without having complete knowledge about the prevalence and mechanisms of poor health outcomes among shift workers.

CONCLUSION

In light of the prevalence of shift work in today's economy and the suggestive research to date about its possible health effects, it is clear that additional research efforts are needed to fully understand health risks and mechanisms through which they arise. The research so far leaves us with uncertainty about the magnitude of the health impacts, the mechanisms through which these impacts occur, individual differences in susceptibility to adverse health outcomes, and the particular forms of shift work that are most troublesome.

In order to get a better sense of these issues, future research should:

- pay more attention to the mechanisms through which shift work affects worker health and safety,
- continue to explore whether some individuals are more susceptible (through genetic predisposition, or current or prior life experiences) to adverse health effects from shift work, and
- measure exposure to shift work much more carefully by clearly distinguishing different types of shift work, and measuring time spent on shift schedules more precisely.