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Vol. 1 No. 3

Fall 1983

ALBERTA OCCUPATIONAL MEDICINE NEWSLETTER

EDITOR'S COMMENTS

In this issue and the next, Dr. Heather Bryant continues her 3-part article on 'Reproductive Hazards of the Workplace'. Because of the space required for the current episode on 'Effects on the Female Worker', we will not have room this time for Dr. G. Jamieson's usual cartoon, but hope to in future issues.

In the next issue, Dr. Bryant's article on effects in male workers will be published, and an article on occupational skin problems.

This Newsletter is produced with financial assistance from the Department of Workers' Health, Safety and Compensation. It aims to be independent and province wide in perspective; it therefore has an Editorial Board, whose members are listed on the back page.

John Markham

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ANNOUNCEMENT

Dr. J.W. Markham, F.R.C.P.(C), as Clinic Director, announces the opening of an Occupational and Environmental Dermatology Clinic at the University of Calgary Medical Clinic, 3350 Hospital Drive, N.W., Calgary, Alberta T2N 4N1.

This will be held weekly on Wednesdays at 8 - 12 a.m. by appointment only, starting on November 23rd, 1983. Telephone 270-3197.

Dr. Kirk A. Barber, M.D., F.R.C.P.(C), Consultant Dermatologist, will be in attendance.

REPRODUCTIVE HAZARDS OF THE WORKPLACE PART 2 EFFECTS ON THE FEMALE WORKER

Heather Bryant, B.Sc., M.D., C.C.F.P.

When the topic of reproductive hazards at work is addressed, the focus is usually on hazards to the female worker, and particularly to the pregnant worker. Employers and employees share the concern about what effect new technologies, chemicals, and other exposures could have on the "innocent" third party in the employment relationship: the fetus. Because it is now more common for pregnant women to continue to work, the presence of the fetus in the workplace is being strongly felt. Thus, it is natural that this concentration has occurred. Much of this article deals with this particular area of a large topic: How do various work environments during pregnancy affect fetal outcome?

A cautionary note, however, should be made before beginning a brief summary of what is known about a selected number of commonly discussed exposures. The study of reproductive hazards should include the study of a wide spectrum of outcomes, as well as a thorough knowledge of the agents of exposure. Thus, menstrual irregularity or dysfunction, infertility, and loss of libido (the last two in males in well as females) should be studies as well. To a large extent, however, they are not. Perhaps because they are somewhat more difficult to document or measure, or perhaps because they seem less immediately dangerous than the prospect of damage to an already existent embryo, these topics are not as thoroughly researched or discussed. It should be kept in mind, however, that the presence of a fetus is not required for reproductive damage to occur.

This part of the series of articles proposes to look at the hazards the worksite may contain for the reproductive health of the female worker. First, a general overview of what is known about the effect of work itself will be given, followed by a discussion of some specific agents which may be encountered, and what is known about their individual effects.

Working in pregnancy: Is there a risk?

This question is obviously difficult to answer unequivocally. While some jobs may involve real physical dangers, others may be considerably less physically demanding than caring for two small children in a typical suburban home. It is worthwhile, however, to attempt an answer to this question, for several reasons. First, understanding how the overall dynamics of work (both traditional employment and domestic responsibilities) affect pregnancy would be of great benefit to the physician advising the patient about her activities during the prenatal period. Should a woman, for example, be encouraged to take employment leave if fatigue becomes a problem? Or should she be encouraged to request lighter tasks or slightly longer rest breaks while continuing her job? Perhaps she should continue her work and be encouraged to seek domestic help. At present, we don't have answers to these questions, beyond our own common sense, and the opinions of experts (based largely on their own common sense[1]).

Another reason for approaching this question is somewhat less directly practical, but applies to how the information currently available should be interpreted. In most occupational studies, the "healthy worker effect" is assumed to be operating: that is, it is assumed that those who are employed are healthier in general than those who are not. This assumption has repeatedly been shown to be true in studies of cohorts of male workers; this is probably because a substantial propor-

tion of the non-working male population is only unemployed because the men are not healthy enough to hold a job. With women, however, this is not necessarily true. In fact, when reproductive health is considered, the reverse may be true. Put most simply, healthy women tend to work today as well, but probably the largest single factor keeping women out of the workforce is not ill health, but a choice to stay home with children. Thus the group of "unemployed" women is heavily populated with the reproductively healthy: those who do not have children, through choice of due to reproductive impairment, continue to work. Do we then have an "unhealthy worker effect"? This is a possibility that should be kept in mind when cohort studies using comparisons of employed groups of women are done: are we in fact considering the possibility that working women are already at a selection disadvantage before the study has begun?

Several approaches have been taken, then, to try and delineate the relationship between work in general and pregnancy outcome. A cross-cultural review was made, for example, of over two hundred traditional societies to examine usual work patterns of women pre- and post-natally.[2] When it was found that most surveyed societies encouraged maintenance of usual duties up until delivery, it was argued that the current trend to employment during pregnancy was evidence of a return to a "normal" social pattern. However, as has been argued in response to this suggestion, just because a pattern of work is traditional, it does not mean that it is beneficial.[3] Studies of pregnancy outcomes would be necessary to answer this question.

British studies addressed this problem several decades ago, with conflicting results. While some studies showed that prematurity rate increased with the duration of paid work[4], even when social class confounding was considered[5], others were unable to show this.[6] A Canadian study showed increase in prematurity with "non-sedentary" employment only.[7] More recent analyses of older British data found low birth weight infants were born more frequently to women who were "gainfully employed" at the start of pregnancy[8], but noted that his could have been due to the increased frequency of smoking amongst the workers. Finally, an American study recently reported (but based on data collected before 1966) found infants of women who worked in the third trimester weighed 150 to 400 grams less than newborns of non-working women; the decrease was greater in women whose work required standing.[9] While smoking and socioeconomic status were controlled for here, the use of data from a time period well before the recent upsurge in female employment makes extrapolation to today's workforce uncertain.

The outcome of spontaneous abortion in workers versus non-workers has also been addressed. A Finnish population-based study did find a slight decrease in spontaneous abortion risk among housewives, but did not control for age, obstetrical history, or even ascertain actual employment status during pregnancy.[10] A retrospective study asking working and nonworking Iranian women about their obstetrical histories also reported increased risk amongst the working group.[11] However, the recall error may have been substantial (average gravidity was 9 for controls and 7.4 for workers); the time of recall often exceeded twenty years.

Thus, there is no clear answer to the question posed in the subtitle to this section. It is hoped that this question can be answered in the near future by doing detailed epidemiological studies of pregnancy outcomes using comprehensive, relevant employment histories and controlling for any possibility of an "unhealthy worker effect".

Selected agents and their effects on reproduction

Lead

It is perhaps fitting that lead be discussed first, as it is probably the first known occupational reproductive hazard. Known as a general toxin for two thousand years[12], lead has in fact historically been used an an abortifacient.[13] In the nineteenth century, miscarriage rates of 52 to 74 percent were reported amongst lead workers.[14] So widely known was it that lead was a risk to pregnancy that women in England were denied employment in white lead production areas.

Lead does cross the placental barrier in animals, even at low maternal blood values[13], and correlations between human maternal and cord blood levels have been shown.[15] The exposure to lead during pregnancy has been linked to subsequent neurotoxicity and mental retardation in the infant.[16]

How significant a problem does this present to the current Canadian working population? While the number of workers exposed to lead in Canada has not been estimated, Canada is a leading world producer of lead ore and refined lead, and recent instances of high industrial lead emissions and significant worker exposures have occurred in this country.[17] It would be well, therefore, to be aware of the potential toxicity of lead to the fetus and to work towards minimal exposures for all workers. (The effects of lead on male reproduction will be discussed in the next issue.)

Waste anesthetic gases

Few agents suspected of causing poor reproductive outcome have sparked as many studies as those on waste anesthetic gases. The research continues principally because this is a most complex exposure to study. The usual study technique is to compare reproductive histories of women (or men) working in operating rooms or dental offices using anesthesia to another similar group of people without this work experience. When differences are found, the gases are presumed to be the toxins. However, some have suggested that this is methodologically questionable: many different gases are used in operating rooms, for example, and to lump all gases together as one may be an over-simplification. In addition, exposures to infection, fatigue, and job stress have been suggested as possible partial explanations or confounders for any relationships found.[18] However, there is substantial evidence to imply that chronic exposure to anesthetic gases is detrimental to a pregnancy, particularly when spontaneous abortion data is collected.

The original work on this topic was done by Vaisman, who reported that of 31 pregnancies occurring to female Russian anesthesiologists, 18 spontaneous abortions occurred, and 2 women discontinued work because of threatened abortions.[19] Work has since been done by Cohen[20], who in a personal interview series of 67 O.R. and 92 general duty nurses found a past spontaneous abortion rate of 29.7 percent in the former group, compared with 8.8 percent in the latter. It is not certain whether these miscarriages occurred in pregnancies actually exposed to anesthetic gases, however; further, the average age of the "exposed" cohort was 3.4 years greater than that of the control group, which may be partially responsible for the difference.

Mailed questionnaire studies have been frequently done to examine this question. A study of British female anesthetists found a small but significant increase in spontaneous abortion rate (18 vs. 15 percent) when exposed versus non-exposed pregnancies within the same group were compared.[21] A survey amongst chairside dental assistants found a 2.3-fold increase of spontaneous abortion amongst women classed as heavily exposed in the year prior to conception.[22] The latter paper implied that nitrous oxide was the most likely responsible agent, whereas an Indian study, where ether is the most common volatile agent, also showed an increased risk.[23]

It would seem, then, that the data argues for an association between miscarriage and anesthetic exposure. However, some studies have reported no significant difference in abortion rates between groups of exposed and non-exposed female physicians, once the data is age-adjusted.[24] A most interesting recent study from Sweden used that country's extensive centralized records system to follow-up the non-respondents in their fairly typical mailed questionnaire.[25] A small but insignificant increase in spontaneous abortion rate was found when employees in high exposure areas during the first trimester were compared with those unexposed during pregnancy, once age and smoking habits were controlled for. Most interesting, however,

was their finding that while only two-thirds of the miscarriages occurring in unexposed pregnancies were reported, virtually all of those occurring in exposed pregnancies were reported. The authors argue that a participant selection bias to report spontaneous abortions preferentially when an adverse exposure is believed to have occurred, may have influenced the outcome in many of the mailed studies.

The incidence of congenital malformations in these studies is difficult to ascertain, as the data are often not presented so that types of malformations, or even major versus minor malformations, can be compared.[26] However, even with this provision, most studies did not demonstrate any significant differences.[21,23,24]

In summary, the studies done have been retrospective and prone to recall and selection bias. Specific exposures have not been documented. However, the bulk of the evidence would seem to indicate an increase in spontaneous abortion rates amongst exposed women; congenital malformations in surviving pregnancies do not appear to present a problem.

Laboratory work

In the mid-seventies, "clusters" of malformed infants or miscarriages occurring to female laboratory workers in Sweden were reported to their National Board of Health and Welfare. Studies done subsequent to this did seem to lend some substantiation to this association: A small study on spontaneous abortions amongst 56 laboratory workers showed a borderline significance of increase in miscarriages amongst the pregnancies exposed to laboratory work.[27] Smoking, age, and family history were all found to confound the relationship.

A later study assembled a "cohort" of 245 deliveries which had occurred to women who had worked at laboratories while pregnant.[28] Malformations recorded on hospital records were checked with the Swedish national register; "expected" rates calculated were corrected for lower parity and higher average age of the mothers when compared to average Swedish mothers. Twenty-nine malformations were found when seventeen were expected, with much of the increase in major malformations. A specific increase in intestinal atresia or stenosis was noted. Because the cohort studied was so small, this was followed by a case-control study of 163 women who had borne infants with gastrointestinal atresia.[29] Occupational histories were derived from case records (for cases) and from mailed questionnaire (controls). An increase in laboratory work reported during pregnancy was found amongst cases (seven found when two were "expected").

The above studies suffer from problems with case ascertainment (newborn registries of defects are far from perfect) and in the latter study, differences in technique of ascertaining occupation between cases and controls may well have biased results. The most difficult problem, however, is to define what particular exposures in the very diverse group called "laboratory workers" were common to the cases. This has not been done. In addition, it should be pointed out that even the authors of the last cited paper estimate the risk to be "probably not very great".[29] Thus, larger studies where specific exposure agents (solvents, other chemicals, and viral exposures being commonly mentioned) are detailed will be necessary before any attribution of increased risk can be made.

Exposure to viruses

In the wake of the discovery of rubella as a teratogen, one would expect studies of workers at high risk of all viral exposures would be done to detect abnormal pregnancy outcomes. An initial Canadian study did address this question by studying the outcomes of pregnancies to nurses who had worked with children, especially those with congenital infections.[30] There was an increase in unspecified types of congenital malformations reported by nurses who had worked with infants, when compared to those not so exposed. However, the study had an extremely low response rate (54%), and no effort was made to validate reported diagnoses or look for malformations in infants reported as normal. One would expect a strong response bias here: women who worked with infants with congenital malformations would be expected to be much more sensitive to the diagnosis and reporting of defects amongst their own children (the data seem to support this hypothesis of bias in this subgroup). This study did not show a relationship between miscarriage and employment exposure.

Cytomegalovirus (CMV) infection amongst women working with children has been more recently studied.[31] Seropositivity and seroconversion rates were found not to be different when 292 women working with children were compared with 163 women in an unexposed group. A substudy in the same paper compared 36 mothers of infants with congenital CMV infection with 36 controls; no increase in child-nursing work was found. This study, although based on a small sample, recommended no particular precautions were required for CMV-seronegative women employed in child care professions. The conclusion that CMV is not a serious occupational risk was also concurred with in a recent brief review.[32]

Video display terminals

This topic is included in this short article not because of the wealth of well-documented information on the subject, but because of recent public interest in the possibility that VDTs may be harmful to a pregnancy. For a more complete, but still brief review, the reader is referred to an article recently published in the Bulletin of the Hereditary Diseases Program of Alberta[33], and recommended in the editorial printed in the first issue of this bulletin.

Public interest in VDTs as a potential hazard was first raised in 1980, when four women working with VDTs at the Toronto Star reported giving birth to sons with abnormalities.[34] This was followed by a report of seven federal government employees exposed to VDTs during pregnancy who had poor reproductive outcomes: four spontaneous abortions, one premature delivery, and two infants with respiratory diseases.[35] Followup studies on the terminals in the involved worksites found radiation emissions from the VDTs so low as to not present a significant hazard.[36]

It is difficult to draw any conclusions of risk when reports of "clusters" such as this are made; one would expect a certain number of such small clusters to occur by chance, and the current sensitivity to VDT exposure would make preferential reporting of abnormalities amongst these workers quite possible. Cohort studies have been proposed, but have proven difficult to undertake due to methodological and practical considerations.[37] Meanwhile, union contracts are now being negotiated which allow women working with VDTs to request transfer to another job.[38]

Currently, then, no solid epidemiological evidence available states that VDTs present a hazard to pregnancy. Radiation emissions from the machines tested appear negligible. Thus, there is no reason for physicians to caution pregnant patients against VDT exposure at present; however, studies directed towards finding a definite answer to this question of risk would be most welcome.

Future work

There is much more work to be done in this area of study. The current focus on the fetus is to be expected, but study of a wider spectrum of outcomes, which include pre-conceptional problems such as those with menstrual function and fertility, are needed as well. There are surprising deficiencies in understanding the effects of employment itself on pregnancy which need to be addressed. Finally, only a fraction of the work needed on specific exposures in the workplace has been done. Many of the workplaces where toxins may be expected to occur are unstudied; in many where studies have been undertaken, the conclusions and recommendations arising from the work are unclear. Finally, the emphasis on the pregnant worker has largely ignored possible effects on the reproductive integrity of male workers. It is the latter subject which will be the focus of the next and final part of this series.

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