Introduction

The symposium was organized by Dr. Bonde and his co-workers from the Department of Occupational Medicine of the University of Aarhus and was sponsored by the European Union (EU) within the Biomed II project “Concerted Action on Occupational Hazards to Male Reproductive Capability,” the Danish Medical Research Council, and the ICOH Scientific Community on “Reproductive Hazards in the Workplace.” The excellently organized meeting was attended by some 100 experts from 15 countries.

The aim of the symposium was to review current hazards to male and female reproduction and to present recent and ongoing studies on this topic; the symposium also offered the opportunity to present the (partly preliminary) results of the EU multicenter study on occupational hazards to male reproductivity. In a satellite symposium, results and strategies of the EU project were discussed in more detail.

Subjects, definitions, and methodology

The main subjects of the symposium were epidemiologic methods used to investigate the time to pregnancy; new approaches in studies of the environment and male and female fertility; preventable causes of infertility related to lifestyle and occupation; and temporal and regional variation in subfertility.

By definition, fecundity is the biologic ability of an individual or couple to conceive and fecundability is the probability of conceiving within a menstrual cycle or month of unprotected intercourse (Juul, DK). With regard to methodologic questions it was pointed out that a practicable approximative measure of fecundity as well as of infertility (i.e., the probability of not getting pregnant within a given period, e.g., 12 months, according to the WHO) is “time to pregnancy” (TTP). TTP studies may be performed as prospective as well as retrospective studies.

The results may be influenced by various factors related to study design and methodology, such as:

1. Eligibility of any recognized pregnancy or of live births only
2. Eligibility of any pregnancy or of the first or last pregnancy only
3. Intention of couples for pregnancy
4. Contraceptive measures before unprotected sex
5. Ignorance of contraception
6. Eligibility criteria of couples, e.g., pregnancy planners only
7. Coital frequency

Influencing factors related to the couples studied and to the environment may be:

1. Coital time relative to ovulation
2. Age of the partners
3. Parity
4. Duration of the partnership

Causes of bias may be:

1. Different behavior in pregnancy planning of exposed and nonexposed groups
2. Change in behavior in response to fertility problems
3. Time trend of exposure resulting in stronger affection of women with a long TTP
4. Recall of the TTP in women and men
5. Calender time
6. Misclassification of exposure (may differ at the time of formation of target cells, the time of conception, and the end of pregnancy)
7. Medical treatment
8. Subfertile worker effect, as women without fertility problems tend to leave the work force more often due to pregnancy and rearing of children than do subfertile women

9. Recruitment bias, as couples with fertility problems are more likely to choose other couples to participate in studies

10. Recall of the waiting time (i.e., TTP), as short TTP periods may be more accurately recalled than long TTP periods

11. Type of recognition of pregnancy

12. Allowing for and recognition of stillbirths

13. Type of and waiting time for truncation of the TTP curve (Spira, F; Olsen, DK; Keiding, DK)

Despite such uncertainties, questionnaires on the TTP in retrospective studies may be quite reliable, at least on a group basis, as compared with data collected from structured interviews or prospective approaches; nevertheless, Baird (USA) encourages additional methodology studies of reliability and validity wherever feasible. Questionnaires should be kept simple and should avoid intimate questions such that couples are not refrained from joining the study. No major difference in recall of the TTP by women or men could be seen; recall is more reliable when given in months than when expressed in cycles. The TTP is mainly negatively correlated with an age of the mother of over 30 years and with smoking by the mother or father, with a bias due to the social situation of the parents being possible (Joffe, UK).

Bonde (DK) raised the question as to how a change in semen quality would translate to changing fecundity at the population level. Applying different statistical models, he showed that under the assumption of a multiplicative model, even a major change in sperm count would not influence fecundability to any significant degree. In contrast, in an additive model, even a small decline in sperm count can result in a serious loss of fecundity and fertility. The nematocide dibromochloropropane (DBCP), which has been proven to lead to serious declines in sperm count and fertility, probably follows an additive pattern.

**Clinical and laboratory methods**

On the basis of initial results of an ongoing Danish prospective study of first-pregnancy planners, Bonde (DK) concluded that changes in sperm count according to the season, duration of sexual abstinence, and age rather follow a multiplicative pattern. It remains to be seen how exposure to substances other than DBCP may affect the sperm count.

For assessment of the chromatin structure of sperm, the flow cytometric sperm-chromatin structure assay (SCSA) was evaluated as being a valuable test. It only weakly correlates with other andrologic parameters, and it seems stable intraindividually over time. Within the framework of the EU project, no significant finding could be seen in longitudinal studies conducted in farmers before and after the pesticide-spraying season or in styrene-exposed workers before and within 12 months of hiring (Spano et al. E).

Aneuploidy in sperm cells can be detected by fluorescence in-situ hybridization (FISH). Some patterns of chemotherapy are shown in the literature to increase the rates of aneuploidy, and so does diazepam poisoning; in these cases the abnormal findings returned to normal within about 100 days. Cigarette smoking, alcohol and caffeine consumption, and age have been associated with unbalanced chromosome numbers. Some fungicides have been reported to increase hyperploidy, but preliminary results obtained by FISH in about 60 farmers investigated in the EU study did not reveal abnormal findings (Lähetie et al. SF).

Larsen (DK) has pointed out that computer-assisted semen analysis (CASA) reduces the interobserver variation significantly. The computer follows the tracks of sperm cells. In the Danish first-pregnancy planner study a higher side-movement velocity of sperm cells is associated with a higher degree of fertility. Various CASA parameters are interdependent, such as sperm velocity and the number of motile sperm cells.

**Menstrual cycle, sperm count and fecundity**

Baird (USA) gave a review on the characteristics of fertile and infertile menstrual cycles. In a prospective study on the hormone patterns of pregnancy planners using continuous blood and urine sampling and analysis of hormone levels or hormone metabolites during all phases of the menstrual cycle until conception, her working group found out that fecundity was positively correlated with high preovulatory luteinizing hormone (LH) levels (contrary to the findings of other working groups) and was negatively correlated with low midluteal levels of LH and progesterone and with high follicular levels of progesterone. Long follicular phases were correlated with loss of fecundity, and higher LH levels were seen in cases of loss of embryo.

Nonfertile men have higher rates of sperm counts below 20 million/ejaculate, but despite this finding, male fecundity does not correlate with the sperm count. The sperm production correlates positively with the number of Sertoli cells. This number is modulated by follicle-stimulating hormone (FSH) and other factors in the neonatal testis (Sharpe, UK).

**Confounders in sperm analyses**

Numerous lectures have reviewed the current knowledge on changes in sperm quality and its causal relationship.