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ORIGINAL RESEARCH

The Participation of Prospective Fathers in Preconception Care

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Abstract: We present the data of male participants in the Coordinating Center of the Hungarian Preconception Service (HPS), Budapest, 1984–2010. One of main objectives of the HPS was the incorporation of male partners of female participants into the preparation of childbirth. The HPS is based on three steps: (I) Reproductive health check-up. (II) A 3-month preparation for conception with the major determinants of the development of new life such as sex, health and/or some diseases. Smoking and illicit drug use cessation and limitation of alcohol intake was suggested in the male participants (III) to achieve optimal conception and better protection of early pregnancy. Pregnant women usually visit prenatal care clinics between the 7th and 12th gestational week when it is too late to reduce the risk of congenital abnormalities. Male participation in HPS will help to enhance use of appropriate preconception methods at the appropriate time.

Keywords: preconception care, male participation, reproductive risk, genetic diseases of prospective fathers, paternal age, sperm examination

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Introduction

In earlier times the division of labor was the following: the males did the "production", the females the "reproduction". The reproducing function of females was extremely important due to the very high early mortality rate, eg, every third infant died during the first postnatal year and only half of the surviving children reached adulthood in Hungary during the 19th century.[1] Thus, the life of females was mainly determined by their reproductive function including menstruation, gestation and lactation, while males only invested short time and energy to conceive offspring via spermatogenesis and sexual intercourse.[2] These different functions in reproduction are likely to have contributed to male chauvinism/dominance in sexual and social life.

Recently, however, the previous division of labor between males and females has drastically changed. At present, females have nearly similar social activities to males outside their homes but they also have to fulfill traditional feminine roles. The consequences of this change are well known and include a robust drop of number of children per family and increasing maternal age. In previous centuries about 70% of a woman's life was connected with reproduction, while at present this figure is estimated at approximately 7%.[3] Thus, prospective fathers may play an increasing role in reproduction. The development of responsible fatherhood is important for optimal conception. However, in general the majority of males have limited knowledge of reproductive health,[4] therefore, their involvement in preconception care may help to improve the efficacy of their participation in reproduction.

The Hungarian Preconception Service (HPS) was established in 1984.[5] There were two reasons for the introduction of HPS. The first reason was a reaction to a very unpopular obligatory premarital counseling that started in 1974, which lacked scientific basis and concentrated only on contraception. The HPS wanted to provide a better alternative medical infrastructure for prospective parents. The second reason was that there was a high need for family planning counseling among couples with low genetic risk due to the popular family planning program in the Hungarian State TV.

There were several objectives of HPS.[5] One objective was increased involvement of male partners in the preparation of their female partner's pregnancy. The present paper focuses on this first objective, examining the participation of male partners in the HPS, and the impact this participation has on different medical aspects of their involvement in preconception care.

Material and Methods

The HPS was planned as part of the primary health care based on qualified and trained midwives after completing a special training course. Midwives were chosen as opposed to doctors because this was more cost-effective, and they were willing to follow the time consuming protocol of the HPS. The task of the midwives in the HPS was to select couples who are at risk for secondary care performed by specialists.

There are three criteria for participation in the HPS: (i) no infertility (defined as no conception after more than 12 months of sexual activity without contraception), (ii) no current pregnancy and (iii) voluntary participation.

The protocol of the HPS includes three steps:

I. Check-up of reproductive health. This includes a preconception screening of reproductive risk factors at the first visit. The check-up items are shown in Table 1.
II. A 3-month preparation for conception. At the time of conception, the fetus's sex, her/his health and/or several diseases are determined. Thus, it is very important and necessary to prepare for conception. The 3-month preparation for conception begins at the first visit and the different items of this step are summarized in Table 2.

Table 1. Reproductive health check-up.

1. Family history of prospective parents, ie, prospective fathers as well.
2. The woman's pregnancy history.
3. The optimal time interval to achieve conception after previous pregnancy outcomes.
4. Maternal and paternal age.
5. Maternal health conditions.
6. Preconception screening of STI/STD in women.
7. Sperm analysis of males.
8. Psychosexual assessment of couples.
9. Check the protection against rubella in prospective mothers.
10. Vaccination against varicella and influenza in prospective mothers.

Table 2. The 3-month preparation for conception.

1. Discontinuation of oral contraception and the use of intrauterine devices in females. Condom use is recommended.
2. Protection of germ cells in couples.
3. Avoidance of occupational hazards in prospective mothers.
4. Check-up of sex-hormonal status of females.
5. Start of periconception folic acid containing multivitamin supplementation in prospective mothers.
6. Recommendation that dental status of females is checked.
7. Guidelines for healthy diet.
8. Guidelines for optimal physical exercise of prospective mothers.

III. To achieve "optimal" conception and to provide a better protection of early pregnancy (Table 3). In general, pregnant women visit prenatal care clinics between the 7th and 12th gestational week. By that time, the embryo has passed through his/her most sensitive and vulnerable period; therefore it is too late to protect it from birth defects. The start to achieve conception is after the second visit while the confirmation of pregnancy is at the third visit in the HPS.

The main results of the HPS regarding female participants were reported previously.[5] In the current report, only the data of male participants are presented.

Results

The HPS included the coordinating center in Budapest and 34 regional centers; however, here only the data of the coordinating center between 1984 and 2010 are shown. The number of female participants was 25,313; of these, 20,603 (81.4%) had male partners who visited the HPS at least once.

Table 3. To achieve "optimal" conception and to provide a better protection of early pregnancy.

1. Evaluation of the results of requested medical examinations of females and males.
2. Continuation of multivitamin supplementation in prospective mothers.
3. Achievement of "optimal" conception.
4. Confirmation of pregnancy in females.
5. Avoidance of teratogenic and other risks.
6. Important further information for pregnant women.

Mean age of participants increased from 29.5 to 35.9 years during the study period of 1984–1989 to 1998–2010. There was a drastic increase in the number of unmarried males (1984–1989: 8.5% and 1998–2010: 29.1%) while the proportion of highly educated males decreased (1984–1989: 77.7% and 1998–2010: 44.4%). Most participants (97%) lived in Budapest and other industrialized towns.

The "genetic check-up" of prospective fathers

This preconceptional screening of possible genetic risk in prospective mothers and fathers was based on an evaluation of their medical history and pedigree; however, here only the data of fathers are mentioned. Of 20,603 prospective fathers, 111 (0.5%) had disorders caused by major mutant genes (most frequently polycystic kidney disease), chromosomal aberrations (47, XXY), structural birth defects (such as undescended testis and cardiovascular malformations) or disabilities (blindness and hearing loss). These individuals were referred to the genetic counseling clinic for further genetic examination and counseling. A chromosomal examination of males was also recommended if their female partners had previous unsuccessful pregnancies, the most frequent type being repeated miscarriages. In addition, in the families of 53 male participants there was an obvious cluster of common complex diseases (cancer, hypertension-stroke, myocardial infarction, diabetes mellitus, depression, etc.); therefore a visit at the genetic counseling clinic for full genetic screening was also recommended.

Paternal age

Of the 20,603 male participants who attended the HPS during the study period, 3,333 (16.2%) were over 40 years, while 1,220 (5.9%) exceeded 50 years.

The advanced age of fathers is associated with a mild increase in reproductive risk including a higher risk of some autosomal dominant disorders, such as achondroplasia and Apert syndrome, and with a somewhat higher risk of some structural birth defects, eg, congenital cardiovascular malformations.[6] However, in spite of the theoretically well-defined higher risks for genetic disorders in the offspring of older fathers, the clinically recognizable risk is not high. Therefore, advanced paternal age was not a reason to refer these prospective fathers to a genetic counseling clinic.

However, this risk was discussed with these couples and special attention was suggested at the ultrasound imaging of fetuses in the 18th–20th gestational weeks for these potential disorders.

Sperm analysis of males

After the collection of data regarding the history of previous conceptions and genitourinary infections of male participants, HPS co-workers suggested a voluntary semen analysis in all males (to obtain the sperm at home by withdrawal or masturbation method after 3 days of sexual abstinence and to provide this sample for laboratory analysis within 1–3 hours). If pathospermia was detected, the examination was repeated and males with confirmed diagnosis were referred to the andrologist of the HPS for final diagnosis and treatment.

15,680 (76.1%) of the male participants who provided sperm for analysis yielded unexpected results. A lower mean number of spermatozoa were found in male participants in the first few years of participation at the HPS compared to the Hungarian baseline figure, and this was followed by a drastic drop in sperm density until 1993 (Table 4). Later further decrease was not observed, but 23% of male participants had less than 20 M/mL of spermatozoa in their total material. The data of motility and teratoid sperm cells are shown in Table 5. The mean proportion of spermatozoa with good motility was between 67% and 71% between 1984 and 2010 without significant change in their annual figures, but 12% of males had asthenospermia (40% or less mobile sperm cells). There was a significant increase in the proportion of teratoid spermatozoa from 11% to 31% between 1984 and 1993, but it did not increase later.

A special test (o-toluidin staining) was used for the detection of pyospermia between 1984 and 1993.[7] Of 15,680 males, 2,540 (16.2%) had pyospermia. Of these 2,540 males, 2,444 (96.2%) had female partners with sexually transmitted infections (STI) or diseases (STD). These couples were also referred to secondary care experts and the members of these couples were treated in parallel.

Finally 35% of males were referred to the andrologist of the HPS, and the early treatment of male infertility resulted in conception in many couples within one year (Table 6).

Table 4. The sperm density of the Hungarian healthy males in the years of 1965–1966 as referenced and in the male participants of the HPS between 1984 and 1993.

Years	Number of males	Number of spermatozoa (Millions/mL)	
		Mean	S.D.
1965–1966	50	74.0	11.5
1984	360	54.8	36.6
1985	423	55.5	30.6
1986	825	49.7	30.1
1987	734	44.8	22.9
1988	600	39.8	20.2
1989	815	37.7	21.8
1990	410	33.6	21.5
1991	428	29.5	17.1
1992	446	33.7	14.9
1993	738	30.3	20.6

Note: Further change was not found after 1993.

Table 5. The mean proportion (%) of spermatozoa with good mobility and teratoid spermatozoa in the Hungarian healthy males in the years of 1965–1966 as referenced and later in the male participants of the HPS.

Years	Number of males	Mean proportion (%) of spermatozoa with good mobility	Mean proportion (%) teratoid spermatozoa
1965–1966	50	71	11
1984–1985	783	68	16
1986–1989	2,974	67	21
1990–1993	2,022	70	28
1994–2010	9,901	68	31

Psychosexual assessment

In the HPS, 12% of the males had premature ejaculation (ie, short intravaginal ejaculatory latency time), but

Table 6. Results of sperm analysis study based on male participants in the HPS between 1984 and 1992 who achieved conception within 1 year.

No. of pregnant women	5,453
No. of male participants with sperm analysis	4,089 (75.0%)
No. of males with pathosperm (less than 20 M/mL and/or 40% motility, more than 50% teratoids, or pyosperm)*	1,124 (27.5%)
No. of males with severe pathosperm (0.1–5.0 M/mL)**	21 (0.5%)

Notes: *Smoking cessation, drug and surgical treatment, AIH; **AID or IVF.

only 3% of couples accepted advice to visit a sexologist. The major explanation for this non-compliance was that they wanted to achieve conception as soon as possible.

Protection of germ cells

Data was obtained regarding the smoking and drinking habits of the prospective parents. Male smokers were informed of the risk caused by smoking for their spermatozoa and sexual activity, the hazard of passive smoking for their partners and planned fetuses/infants, and the importance of solidarity with their partners to have a healthy baby. In addition an educational course was organized for smokers between 1990 and 1998 including two group discussions per week under the direction of an expert during the 3-month preparation period for conception. The rate of female smokers was reduced from 17.9% to 7.9% at the time of conception, and of the male smokers from 24.2% to 18.0%.

The rate of hard (one drink or more per day) and regular (more than one drink per week) drinkers was 8.8% and 65.7% among male participants; thus, reduction of drinking was advised. Couples were also informed about the hazards of cocaine, heroin and other illicit drug use.

Finally 7,765 female participants were evaluated in a validation study between 1984 and 1992, and as it appeared, 6502 (83.7%) followed the protocol of the HSP. However, this proportion was higher in females with male partners (5,041; 91.0%) than in females without male partners (2,724; 70.3%). Benefits of male participation for females included a lower drop-out rate, better understanding of medical methods, and a greater likelihood of fulfilling the HPS protocol in an appropriate amount of time.

Discussion

The involvement of male partners was successful in 81% of the couples in the HSP between 1984 and 2010. The participation of males was important for some medical aspects.

There was a robust decline in the quality of sperm in male participants. The Hungarian baseline figures of sperm were determined in healthy young males (medical students) in 1965–1966, and the mean number of spermatozoa was 74 M/mL.[6] This finding was in agreement with the results of clinical examinations in the 1960s. The sensitivity and specificity of sperm counts are limited for biological and technical reasons; therefore, the combined examination of sperm count, motility and morphology was introduced in the HPS.[7] The sperm analysis of the male participants of the HPS was performed by the same method and by the same assistant;[9] therefore we could not attribute the drastic decrease of sperm count and the increase of teratoid forms to technical differences.

This decline in semen quality has also been observed in some other countries in the second half of the 20th century. Carlsen et al[10] stated that human semen quality declined by about 50% from 1930 to 1991. Swan et al[11] re-examined the reported data and calculated that there were declines of 1.3% per year in sperm density, with secular declines that were strongest in Europe, weaker in North America, and either small or non-existent in other countries (for which data were scarce). In addition, there was a significant increase in the incidence of testicular cancer (mainly in young adults)[12] and a moderate increase in the birth prevalence of hypospadias and undescended testis (cryptorchidism).[13] It was proposed that the above interrelated disorders such as low sperm count, testicular cancer, hypospadias and undescended testis be delineated as testicular dysgenesis syndrome.[14]

The recent drastic impairment of male reproductive health has generated some hypotheses. One of the most accepted hypotheses is connected with endocrine-disrupting agents. The major regulator system of the male reproductive system is the hypothalamic-pituitary-testis (HPT) axis including gonadotropin-releasing hormone (GnRH) in the hypothalamus, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in the pituitary gland, and the Leydig cells (secreting testosterone and estradiol) and the Sertoli cells (producing inhibin B) in the testis. These so-called endocrine-disrupting chemicals can interfere at any level of the HPT axis with the most sensitive period during fetal life.[15] Among the endocrine-disrupting chemicals, there are metabolites of estrogens,[16] persistent DDT metabolite, p,p'-DDE as a potent androgen receptor antagonist,[17] and anti-androgenic phthalates used in perfumes, nail varnishes, hairsprays and other chemicals.[18] In Hungary the massive use of contraceptive pills in females was introduced in 1970s and the decline of sperm quality was observed some years later.[9]

This finding implies that the consumption of female hormone-contaminated water during pregnancy may be dangerous for the development of genital organs of male fetuses.

We have also offered an alternative hypothesis suggesting a decline in male reproductive health.[19] There had been strong natural selection against poor reproductive health in the past, but this selective pressure was relaxed in recent years. For example, in Hungary, the average number of newborn infants per fertile couples was 9 in 1920, while 16% of all Hungarian couples had no child due to their infertility. However, the average number of newborn infants in fertile couples subsequently dropped substantially to 1.3 in recent decades, due to effective birth control. On the other hand, infertile couples have had access to recent effective fertility treatments (artificial insemination, in vitro fertilization, etc.), so most of these couples were able to have children. At present, the rate of childless couples due to biological reasons is about 6% in Hungary. As a result of these changes, the rate of children in the general population born to subfertile couples increased from an extremely low proportion of 1%–4% at the start of the 20th century to about 14%–20% by the end of the 20th century. Because of this contraselective trend, the proportion of men in the population with an inherited origin of subfertility has increased substantially during the period that sperm density has been reported to have declined. We hypothesize that the relaxation of natural selection against subfertility may account for the recent decline in sperm quality, and note that subfertility is also related to the higher risk of hypospadias and testicular cancer.[19]

Paternal age also influences spermatogenesis. With advanced age, the number of germinal cells and Sertoli cells decreases, while Leydig cells become hypertrophic parallel with the sperm count decrease in the semen. However, complete spermatogenesis has been observed in men up to the age of 95 years.[20]

Finally two additional benefits of HPS are mentioned here. The preconception screening of STIs/STDs in female participants in the HPS[21] was complemented by the examination of male partners. In general, STIs/STDs were diagnosed in both members of couples followed by their parallel treatment in the secondary care. The beneficial effect of preconception screening of STIs/STDs with appropriate treatment has been demonstrated by a reduced rate of preterm birth.[21]

One of the major risks for germ cells and the fetus is the smoking of prospective fathers and mothers. The educational course for prospective parents who were smokers during the 3-month preparation period for conception helped to explain several risks of smoking and helped motivate parents to quit. This method was successful for prospective mothers and some prospective fathers.[22]

In conclusion, the involvement of males in the HPS resulted in an earlier detection of male infertility with the appropriate treatment of infertile couples, allowing these couples to achieve conception earlier. Thus, it appears necessary to change the previous definition of infertility. Instead of "no conception after more than 12 months of sexual activity without contraception", this definition may be better termed as "no conception after the recognition and treatment of the female, the male or combined infertility problems during preconception care". In addition, the preconception screening of STIs/STDs of couples including males, followed by effective treatment of these couples, reduced the risk of preterm births. Finally, the integration of a smoking cessation program in the HPS helped some prospective fathers to quit smoking.

Another topic that needs discussion is increasing paternal age. In general, males are older (by a mean of 4 years) than their female partners in Hungary; thus, an increasing maternal age is associated with an increasing paternal age. This trend was observed repeatedly in the HPS during the study period. However, the proportion of males over 35 years (16.2% versus 38.1%) and 40 years (5.9% versus 13.0%) in the HPS was lower than in the Hungarian population; thus, advanced paternal age was not a reason for participation in the HPS.

Gametogenesis involves mitotic proliferations, being meiotic recombination followed by reduction divisions and subsequent differentiation into highly specialized germ cells.[23] These processes are quite different, however, in the germ cells of males and females. The number of mitotic cell divisions during spermatogenesis reaches approximately 150 divisions at the age of 20 years and increases linearly at a rate of about 23 cell divisions per year, to reach 840 divisions at the age of 50.[24] There are only 22 divisions during oogenesis throughout the life of a female.

The duration of meiosis during spermatogenesis is short, only weeks, while it is much longer for female germ cells, up to several decades. These biological phenomena explain the different vulnerability of germ cells to mutagenic factors in males and females. A higher mutagenic risk in older men was shown[25] and was explained by possible causes:

1. There is a reduced activity of anti-oxidant enzymes in seminal fluid and spermatozoa in older men.[26]
2. The ability to respond to mutagens with germ cells' apoptosis to avoid genetically altered spermatozoa decreases with age.[27]
3. DNA repair system is lacking in late spermatids and spermatozoa.[28]
4. The aging males present hypermethylation of ribosomal DNA in spermatozoa.[29]

These biological mechanisms explain the real and possible higher genetic risk in the offspring of older fathers:

A. There is a higher risk of some autosomal dominant disorders, such as achondroplasia and Apert syndrome due to new mutations (single base substitutions) in two specific genes: fibroblast growth factor receptor 2 and 3, ie, FGRF2 and FGFR3. The prevalence of achondroplasia is 1 in 15,000 live births and about 97% of cases are caused by two new mutations at the same site of the FGFR3 gene. The risk of a male aged over 50 years of fathering a child with achondroplasia is 7.8-fold higher than that of a 25–29 year old man.[30] However, this higher relative risk of achondroplasia in the offspring of fathers aged over 50 years means an absolute risk of 1 in 1,923, which is clinically negligible.

   The prevalence of Apert syndrome is 14 cases in 1 million live births, caused by two specific mutations in FGFR2 gene. The risk for Apert syndrome is 9.5-fold higher in a male aged over 50 years than that of a 25–29 year old man.[30]

   Some other autosomal-dominant genetic diseases due to new mutations such as thanatophoric dysplasia type I and II (again mutations of FGFR3 gene), multiple endocrine neoplasia type 2B (caused by RET proto-oncogene), myositis ossificans and Marfan syndrome[30] have an almost exclusively paternal origin. Neurofibromatosis type I, Pfeiffer's and Crouzon syndromes were also found to be connected with the new mutations of paternal origin, but other studies did not confirm this relation. Thus, in men aged at least 40 years, the risk of de novo autosomal dominant diseases was estimated at 0.3%–0.5% by Friedman[31] but others considered this to be an exaggerated figure.[30]

B. The risk of polysomy (eg, Down syndrome) in children of advanced-aged fathers is not higher, though a higher risk of Down syndrome in the offspring of elder fathers has been previously published.[32]

C. A higher rate of structural chromosomal aberrations in spermatozoa of older men was observed,[33] but a higher rate of de novo structural chromosomal aberrations was not found in live-born newborns, stillbirth and prenatally diagnosed malformed fetuses of older fathers.[34]

D. Advanced paternal age is associated with a somewhat higher risk of some structural birth defects, eg, cardiovascular malformations.[35]

E. A somewhat higher rate of mortality including miscarriages, stillbirths and infant mortality was found in the offspring of older fathers.[36]

F. Older fathers need a longer period to achieve conception including in vitro fertilization with a possible higher risk of chemical pregnancy (very early fetal loss).[37]

G. Some studies have shown an association of advanced paternal age with a higher risk of childhood cancer and autism spectrum in addition to some complex diseases such as non-familial Alzheimer's disease, non-familial schizophrenia, and prostate cancer in the children of older fathers. A recent study in Iceland showed that the mutation rate of single nucleotide polymorphisms is affected by the age of the father at the time of the conception of the child. The paternal age effect resulted in an increase of about two mutations per year and an exponential model estimated paternal mutations doubling every 16.5 years. These observations shed light on the importance the father's age has in the risk of diseases such as schizophrenia and autism-spectrum.[38]

H. A shorter life expectancy in children of older fathers is worth considering in prospective fathers over 50 years.

On the other hand, socio-economic advantages for children born to older fathers have also been shown.[39]

In conclusion, in spite of the theoretical well-defined risks for de novo autosomal dominant disorders in the offspring of older fathers, so far the clinically recognizable risks are not high. Thus, the opinion of the American College of Obstetricians and Gynecologists[40] was that advanced paternal age is not a reason to counsel routinely. However, our opinion is that these risks of elder prospective fathers warrant discussion with male participants and their female partners in preconception care, and it is worth recommending a special ultrasound imaging in the 18th–20th gestational weeks of fetuses because of these potential defects.

Conclusions

The main message of this paper is that the involvement of male partners in preconception care is feasible and useful. Experiences in Hungary showed the significant change in male behavior concerning reproduction, eg, in their participation in the preconception care. In addition, the participation of males helped to detect infertility and STIs/STDs earlier, followed by an earlier treatment of the couples. In addition, prospective fathers with specific genetic risks of disorders were frequently recognized and directed to appropriate experts. The participation of males improved the compliance of their female partners in the HPS and increased their self-esteem, helping to achieve a healthy baby.

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Competing Interests

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Author Contributions

Conceived and designed the experiments: AEC. Analyzed the data: BC. Wrote the first draft of the manuscript: AEC, BC, AV. Contributed to the writing of the manuscript: AEC, BC, AV. Agree with manuscript results and conclusions: AEC, BC, AV. Jointly developed the structure and arguments for the paper: AEC, BC, AV. Made critical revisions and approved final version: AEC, BC, AV. All authors reviewed and approved of the final manuscript.

Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. The external blind peer reviewers report no conflicts of interest. Written informed consent to participate was obtained from all study participants.

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