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Paternal Age and Chromosome Abnormalities/Miscarriage

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1. Advanced paternal age and the risk of spontaneous abortion: an analysis of the combined 2011-2013 and 2013-2015 National Survey of Family Growth.

Author(s): Nguyen, Brian T; Chang, Erica J; Bendikson, Kristin A

Source: American journal of obstetrics and gynecology; Nov 2019; vol. 221 (no. 5); p. 476

Publication Date: Nov 2019

Publication Type(s): Journal Article

PubMedID: 31128112

Abstract:BACKGROUNDMaternal and paternal age at first birth are increasing across the global population. Spontaneous abortion, one of the most common abnormal pregnancy outcomes, is known to occur more frequently with increasing maternal age. However, the relationship of advanced paternal age and spontaneous abortion is poorly understood, and previous results have yielded conflicting results.OBJECTIVETo examine the influence of paternal age on the risk of spontaneous abortion among singleton pregnancies conceived without assisted reproductive technologies.MATERIALS AND METHODSThis was a retrospective, case-control study using combined pregnancy data from the Centers for Disease Control and Prevention's 2011-2013 and 2013-2015 National Survey of Family Growth. Spontaneous, singleton pregnancy data from women aged 15-45 years were analyzed. Ongoing pregnancies, induced abortions, ectopic pregnancies, preterm births, and intrauterine fetal deaths were excluded. Bivariate associations of pregnancy outcome (spontaneous abortion at <20 weeks and ≤12 weeks vs. live birth at ≥37 weeks) and paternal age were determined, along with those of maternal age and selected demographic and pregnancy characteristics. Significant associations were included in a multivariable logistic regression, which accounted for multiple pregnancies derived from the same respondent.RESULTSA total of 12,710 pregnancies from 6979 women were analyzed, consisting of 2300 (18.2%) spontaneous abortions and 10,410 (81.8%) term live births. Median maternal and paternal ages were 25 and 28 years, respectively. After adjusting for maternal age, race/ethnicity, socioeconomic status, marital status, and pregnancy intention, pregnancies resulting in spontaneous abortions had 2.05 (95% confidence interval, 1.06-2.20) times the odds of being from a father aged 50 years or older, vs. 25-29 years of age. These relationships remained significant when defining SABs at ≤12 weeks (adjusted odds ratio, 2.30; 95% confidence interval, 1.17-4.52).CONCLUSIONPaternal age may increase the odds of spontaneous abortion, independent of selected factors, including demographics, pregnancy intention, and maternal age. This association was robust across several gestational age-based definitions of spontaneous abortion, even after adjustment.

Database: Medline

2. Evaluating the role of paternal factors in aetiology and prognosis of recurrent pregnancy loss: Study protocol for a hospital-based multicentre case-control study and cohort study (REMI III project)

Author(s): Du Fosse N.; Van Der Hoorn M.-L.; Van Lith J.; Lashley E.; Eikmans M.; Heidt S.; Le Cessie S.; Mulders A.

Source: BMJ Open; Nov 2019; vol. 9 (no. 11)

Publication Date: Nov 2019

Publication Type(s): Article

PubMedID: 31727666

Abstract: Introduction Recurrent pregnancy loss (RPL) is defined as the spontaneous demise of two or more pregnancies before the fetus reaches viability. Despite investigation of multiple known maternal risk factors, in more than 50% of couples, this condition remains unexplained. Studies focusing on paternal factors in RPL are scarce, and therefore, paternal evaluation in RPL is currently very limited. However, regarding single miscarriage, there are multiple publications suggesting a contributive role of paternal factors. In this project, we aim to identify paternal factors associated with RPL and to improve couple-specific prediction of future pregnancy outcomes by developing a prediction model containing both maternal and paternal factors. Methods and analysis In a case-control design, the relation between unexplained RPL and paternal age, lifestyle factors, sperm DNA damage and immunomodulatory factors in peripheral blood and semen will be studied. Prospectively, 135 couples with naturally conceived unexplained RPL (cases) and 135 fertile couples without a history of pregnancy loss (controls) will be included, with collection of paternal blood and semen samples and documentation of clinical and lifestyle characteristics. In addition, 600 couples from both groups will be included retrospectively. To adjust for confounders, multivariate logistic regression will be used. The predictive value of paternal and maternal factors will be studied in the total RPL cohort consisting of approximately 735 couples. The primary outcome of the cohort study is live birth within 5 years after initial visit of the clinic. Secondary outcomes are ongoing pregnancy, time interval until next pregnancy and pregnancy complications. Ethics and dissemination This project is approved by the Medical Research Ethics Committee of the Leiden University Medical Center. No risks or burden are expected from the study. The findings of this study will be disseminated via peer-reviewed publications and presentations at international conferences. Trial registration number NL7762

Database: EMBASE

3. Disentangling the roles of maternal and paternal age on birth prevalence of down syndrome and other chromosomal disorders using a Bayesian modeling approach.

Author(s): Thompson, James A

Source: BMC medical research methodology; Apr 2019; vol. 19 (no. 1); p. 82

Publication Date: Apr 2019

Publication Type(s): Research Support, N.i.h., Extramural Journal Article

PubMedID: 31014243

Abstract:BACKGROUNDMultiple neonatal and pediatric disorders have been linked to older paternal ages. Combining these findings with the evidence that many men are having children at much later ages generates considerable public health concern. The risk of paternal age has been difficult to estimate and interpret because children often have parents whose ages are similar and likely to be confounded. Epidemiologic studies often model the conditional effects of paternal age using regression models that typically treat maternal age as linear, curvilinear or as age-band categories. Each of these approaches has limitations. As an alternative, the current study measures age to the nearest year, and fits a Bayesian model in which each parent's age is given a conditional autoregressive prior (CAR).METHODSData containing approximately 12,000,000 birth records were obtained from the United States Natality database for the years 2014 to 2016. Date were cross-tabulated for maternal ages 15-49 years and for paternal ages 15-65 years. A Bayesian logistic model was implemented using conditional autoregressive priors for both maternal and paternal ages modeled separately and jointly for both Down syndrome and chromosomal disorders other than Down syndrome.RESULTSModels with maternal and paternal ages given CAR priors were judged to be better fitting than traditional models. For Down syndrome, the approach attributed a very large risk to advancing maternal age with the effect of advancing paternal age having a very small sparing effect on birth prevalence. Maternal age was also related to the birth prevalence of chromosomal disorders other than Down syndrome while paternal age was not.CONCLUSIONSAdvancing paternal age was not associated with an increase in risk for either Down syndrome or chromosomal disorders other than Down syndrome.

Database: Medline

4. Advanced paternal age, infertility, and reproductive risks: A review of the literature.

Author(s): Brandt, Justin S; Cruz Ithier, Mayra A; Rosen, Todd; Ashkinadze, Elena

Source: Prenatal diagnosis; Jan 2019; vol. 39 (no. 2); p. 81-87

Publication Date: Jan 2019

Publication Type(s): Journal Article Review

PubMedID: 30520056

Available at Prenatal diagnosis - from Wiley Online Library

Available at Prenatal diagnosis - from Unpaywall

Abstract: Advanced paternal age (APA) is associated with infertility and other reproductive risks. Studies looking at APA and outcomes have used different paternal age cut-offs, which has complicated systematic evaluations of reproductive risk associated with paternal aging. This review of the literature suggests that the impact of paternal aging on adverse reproductive outcomes is small, but significant. Studies suggest the incidence of paternal age effect disorders attributed to de novo autosomal dominant mutations is less than 0.5%. Other risks associated with APA include infertility, miscarriage, birth defects, poor neurodevelopmental outcomes, and childhood cancer. Although the increasing prevalence of APA has mirrored the rise in maternal age, this topic has not received similar attention. In this review, we summarize the available literature on the reproductive risks associated with APA to provide a framework for comprehensive genetic counseling and evidence-based management of APA pregnancies.

Database: Medline

5. Advanced paternal age how does it affect fertility and pregnancy related outcomes?

Author(s): Mirza F.; Khoury S.; Ghulmiyyah L.; Eid J.; Nassif J.A.

Source: Journal Medical Libanais; 2018; vol. 66 (no. 1); p. 41-45

Publication Date: 2018

Publication Type(s): Review

Abstract: When compared to maternal age, paternal age has not attracted the same attention throughout history. Advanced paternal age has been sometimes incriminated as a possible factor that can affect pregnancy and its outcomes. In this review, we discuss the effect of paternal age on fertility, miscarriage, chromosomal abnormalities, congenital anomalies, perinatal outcomes, and neurodevelopmental disorders. In fact, advanced paternal age is associated with decreased semen quality leading to lower pregnancy rates, longer time to conception, and a higher number of miscarriages. Additionally, an increase in the rate of adverse pregnancy outcomes, such as congenital anomalies and preeclampsia, is reported when the father's age is advanced. However, no significant effect on the outcome of assisted reproductive technology (ART) or the risk of trisomies, is confirmed.

Database: EMBASE

6. Paternal age: The considerable confounding risk factor in chromosomal aneuploidies

Author(s): Rajangam S.; Nanjappa L.; Lalitha C.

Source: International Journal of Human Genetics; Dec 2018; vol. 18 (no. 4); p. 267-270

Publication Date: Dec 2018

Publication Type(s): Article

Available at INTERNATIONAL JOURNAL OF HUMAN GENETICS - from Free Medical Journals . com

Available at INTERNATIONAL JOURNAL OF HUMAN GENETICS - from Unpaywall

Abstract: The association of advanced maternal age with chromosomal aneuploidies has been widely discussed and debated over decades. The effect of paternal age was underreported and left room for analysis and discussion. In a retrospective study, the researchers observed the paternal age of three chromosomal aneuploidies from the Indian population. Patient data with confirmed karyotype included the paternal age. The paternal age was dichotomized into two groups (<30 years) and (>30 years). Linear regression analysis was applied to observe the correlation of paternal age with children born with aneuploidies. Interestingly, the researchers could deduce the statistically significant paternal age as a confounding risk factor in chromosomal aneuploidy in both age groups for Down and Turner syndrome. These observations facilitated the need of a strategic approach in the management of couples at risk of cytogenetic abnormalities.Copyright © Kamla-Raj 2018.

Database: EMBASE

7. Reproductive genetics and the aging male.

Author(s): Yatsenko, Alexander N; Turek, Paul J

Source: Journal of assisted reproduction and genetics; Jun 2018; vol. 35 (no. 6); p. 933-941

Publication Date: Jun 2018

Publication Type(s): Journal Article Review

PubMedID: 29524155

Available at Journal of assisted reproduction and genetics - from SpringerLink - Medicine

Available at Journal of assisted reproduction and genetics - from Europe PubMed Central - Open Access

Abstract:PURPOSETo examine current evidence of the known effects of advanced paternal age on sperm genetic and epigenetic changes and associated birth defects and diseases in offspring.METHODSReview of published PubMed literature.RESULTSAdvanced paternal age (> 40 years) is associated with accumulated damage to sperm DNA and mitotic and meiotic quality control mechanisms (mismatch repair) during spermatogenesis. This in turn causes well-delineated abnormalities in sperm chromosomes, both numerical and structural, and increased sperm DNA fragmentation (3%/year of age) and single gene mutations (relative risk, RR 10). An increase in related abnormalities in offspring has also been described, including miscarriage (RR 2) and fetal loss (RR 2). There is also a significant increase in rare, single gene disorders (RR 1.3 to 12) and congenital anomalies (RR 1.2) in offspring. Current research also suggests that autism, schizophrenia, and other forms of "psychiatric morbidity" are more likely in offspring (RR 1.5 to 5.7) with advanced paternal age. Genetic defects related to faulty sperm quality control leading to single gene mutations and epigenetic alterations in several genetic pathways have been implicated as root causes.CONCLUSIONSAdvanced paternal age is associated with increased genetic and epigenetic risk to offspring. However, the precise age at which risk develops and the magnitude of the risk are poorly understood or may have gradual effects. Currently, there are no clinical screenings or diagnostic panels that target disorders associated with advanced paternal age. Concerned couples

and care providers should pursue or recommend genetic counseling and prenatal testing regarding specific disorders.

Database: Medline

8. Association of Parental Age and the Type of Down Syndrome on the Territory of Bosnia and Herzegovina

Author(s): Sotonica M.; Hasic S.; Kiseljakovic E.; Jadric R.; Mackic-Djurovic M.; Ibrulj S.

Source: Medical archives (Sarajevo, Bosnia and Herzegovina); Apr 2016; vol. 70 (no. 2); p. 88-91

Publication Date: Apr 2016

Publication Type(s): Article

PubMedID: 27147778

Available at Medical archives (Sarajevo, Bosnia and Herzegovina) - from Europe PubMed Central - Open Access

Available at Medical archives (Sarajevo, Bosnia and Herzegovina) - from Free Medical Journals . com

Available at Medical archives (Sarajevo, Bosnia and Herzegovina) - from ProQuest (Health Research Premium) - NHS Version

Available at Medical archives (Sarajevo, Bosnia and Herzegovina) - from Unpaywall

Abstract:BACKGROUND: Advanced paternal and/or maternal age is a classic risk factor for Down syndrome. The aim of the study was to investigate the frequency of Down syndrome types in children and its association with maternal and paternal age in Bosnia and Herzegovina.SUBJECTS AND METHODS: The cross sectional, observational study included 127 children, 49 girls and 78 boys, aged 1-180 months suspected to have Down syndrome, admitted to the Centre for Genetics, Faculty of Medicine University of Sarajevo, for cytogenetic analysis and differential diagnosis of Down syndrome during the period from January 2010 to May 2015. Standard method of 72 hours cultivation of peripheral blood lymphocytes has been applied. The accepted level of statistical significance was $p<0.05$.STUDY RESULTS: The most common type of Down syndrome was standard trisomy (86.6%), comparing to translocation and mosaicism (7.1%; 6.3%, respectively). The highest frequency of Down syndrome cases was in mother and father's group from 30-39 years old (57; 57 children, respectively) compared to mother and father's groups with younger than 30 (44; 29, respectively) and 40 and older (26; 41, respectively). The significant difference was found in maternal age between translocation and mosaicism groups ($p=0.036$). Difference between parental years and type of Down syndrome was significant when Standard trisomy 21 and translocation ($p=0.045$), as well as mosaicism and translocation ($p=0.036$), were compared.CONCLUSION: The most common type of Down syndrome was standard trisomy 21, with highest occurrence in parents from 30 to 39 years old. Parents were the youngest in translocation group. Obtained results suggest that multidisciplinary approach to identifying the trigger for trisomy appearance and the influence of maternal age is required.

Database: EMBASE

9. Influence of paternal age on ongoing pregnancy rate at eight weeks' gestation in assisted reproduction.

Author(s): Meijerink, Aukje Marieke; Ramos, Liliana; Fleischer, Kathrin; Veltman, Joris A; Hendriks, Jan C; Braat, Didi D

Source: Reproductive biomedicine online; Jan 2016; vol. 32 (no. 1); p. 96-103

Publication Date: Jan 2016

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 26615900

Available at Reproductive biomedicine online - from Unpaywall

Abstract:A retrospective cohort study was performed with the followings aims: to evaluate the influence of paternal age on best embryo quality available for embryo transfer on the third day; biochemical pregnancy rate; miscarriage rate and ongoing pregnancy rate at 8 weeks' gestational age, after IVF or intracytoplasmic sperm injection (ICSI) treatment, respectively, including treatment with non-ejaculated spermatozoa. In total, 7051 first IVF/ICSI cycles in Radboud university medical center, between 1 January 2001 and 1 June 2013 were included in this study. A statistical model was used to analyse the effect of paternal age and maternal age. No statistically significant differences between the paternal age groups were found with respect to the probability of an ongoing pregnancy after the first cycle (35-44 years: odds ratio [OR] = 0.97 [95% confidence interval [CI]: 0.86 to 1.10] and ≥45 years: OR = 1.01 [95% CI: 0.82 to 1.26]), respectively, compared with <35 years of age (control). Similar results were found with respect to paternal age and the availability of a top quality embryo for transfer, biochemical pregnancy and miscarriage. However, live birth was not taken into account. In conclusion, paternal age did not affect ongoing pregnancy rates in first IVF/ICSI cycles.

Database: Medline

10. Effect of Paternal Age on Reproductive Outcomes of In Vitro Fertilization.

Author(s): Wu, Yixuan; Kang, Xiangjin; Zheng, Haiyan; Liu, Haiying; Liu, Jianqiao

Source: PloS one; 2015; vol. 10 (no. 9); p. e0135734

Publication Date: 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 26352861

Available at PloS one - from Europe PubMed Central - Open Access

Abstract: Although the adverse effects of maternal aging on reproductive outcomes have been investigated widely, there is no consensus on the impact of paternal age. Therefore, we investigated the effect of paternal age on reproductive outcomes in a retrospective analysis of 9,991 in vitro fertilization (IVF) cycles performed at the Reproductive Medicine Center of the Third Affiliated Hospital of Guangzhou Medical University (China) between January 2007 and October 2013. Samples were grouped according to maternal age [<30 (3,327 cycles), 30-34 (4,587 cycles), and 35-38 (2,077 cycles)] and then subgrouped according to paternal age (0.05). Chi-squared analysis revealed that there were no differences in implantation and pregnancy rates among the different paternal age groups when maternal age was 0.05). However, implantation and pregnancy rates decreased with paternal age in the 31-34 y maternal age group (P <0.05). Our study indicates that paternal age has no impact on fertilization rate, embryo quality at the cleavage stage and miscarriage rate. For the 30-34 y maternal age group, the implantation rate decreased with increased paternal age, with the pregnancy rate in this group being significantly higher in the paternal <30 y and 30-32 y age groups, compared with those in the 36-38 y and 39-41 y groups.

Database: Medline

11. Effect of paternal age on reproductive outcomes in oocyte donation model: A systematic review

Author(s): Sagi-Dain L.; Dirnfeld M.; Sagi S.

Source: Fertility and Sterility; Oct 2015; vol. 104 (no. 4); p. 857

Publication Date: Oct 2015

Publication Type(s): Review

PubMedID: 26215757

Available at Fertility and sterility - from Unpaywall

Abstract: Objective To perform a meta-analysis of the literature examining the influence of paternal age on oocyte donation outcomes. Design Systematic review of the literature with no language or time restrictions. Setting Not applicable. Patient(s) None. Intervention(s) None. Main Outcome Measure(s) Pregnancy and live-birth rates. Result(s) By independent screening of titles and abstracts, two investigators selected original studies examining the influence of paternal age on oocyte donation outcomes. Twelve articles were included, encompassing a total of 12,538 oocyte-donation cases. No statistically significant correlation was found by most studies between advanced paternal age and the rate of fertilization, cleavage embryo development, implantation, pregnancy, miscarriage, or live birth. A statistically significant decrease in blastocyst embryo formation was suggested in two articles. Except for volume and possibly motility, other sperm characteristics such as concentration and morphology did not alter with age. However, the overall quality of the evidence was rated as very low according to Grading of Recommendations Assessment, Development, and Evaluation criteria. Conclusion(s) The available evidence suggests that advancing paternal age is not associated with adverse oocyte donation outcomes, including pregnancy and live-birth rates. However, the suboptimal quality of the available evidence necessitates high-quality, well-adjusted prospective trials that are also aimed at evaluating additional outcomes such as congenital anomalies and various specific long-term disorders.

Database: EMBASE

12. Pregnancy with advanced maternal and paternal age

Author(s): Schenker J.G.

Source: Journal of Perinatal Medicine; Oct 2015; vol. 43

Publication Date: Oct 2015

Publication Type(s): Conference Abstract

Available at Journal of Perinatal Medicine - from Unpaywall

Abstract: Delayed child-bearing, which has increased greatly in recent decades. Many women are unaware of the success rates or limitations of assisted reproductive technology and of the increased medical risks of delayed child-bearing, including multiple births, preterm delivery, stillbirth, and Caesarean section. It is reasonable to expect in the next decade that the options to preserve oocytes and oocytes donation programs child-bearing at advanced maternal age will expand. Increasing male age is related with decreasing percentages of progressively motile sperm and morphologically normal sperm, but not obviously with the rates of fertilization, good quality embryo, implantation, Father's age increase miscarriage, malformations, risks of autism, schizophrenia, and bipolar troubles in children. . Possible biological mechanisms include de novo aberration and mutations or epigenetic alterations associated with male aging. Care providers need to be aware of these complications and adjust obstetrical management protocols to ensure optimal maternal and perinatal outcomes.

Database: EMBASE

13. Male biological clock: a critical analysis of advanced paternal age.

Author(s): Ramasamy, Ranjith; Chiba, Koji; Butler, Peter; Lamb, Dolores J

Source: Fertility and sterility; Jun 2015; vol. 103 (no. 6); p. 1402-1406

Publication Date: Jun 2015

Publication Type(s): Journal Article Review

PubMedID: 25881878

Available at Fertility and sterility - from Unpaywall

Abstract: Extensive research defines the impact of advanced maternal age on couples' fecundity and reproductive outcomes, but significantly less research has been focused on understanding the impact of advanced paternal age. Yet it is increasingly common for couples at advanced ages to conceive children. Limited research suggests that the importance of paternal age is significantly less than that of maternal age, but advanced age of the father is implicated in a variety of conditions affecting the offspring. This review examines three aspects of advanced paternal age: the potential problems with conception and pregnancy that couples with advanced paternal age may encounter, the concept of discussing a limit to paternal age in a clinical setting, and the risks of diseases associated with advanced paternal age. As paternal age increases, it presents no absolute barrier to conception, but it does present greater risks and complications. The current body of knowledge does not justify dissuading older men from trying to initiate a pregnancy, but the medical community must do a better job of communicating to couples the current understanding of the risks of conception with advanced paternal age.

Database: Medline

14. An unexpected finding: younger fathers have a higher risk for offspring with chromosomal aneuploidies.

Author(s): Steiner, Bernhard; Masood, Rahim; Rufibach, Kaspar; Niedrist, Dunja; Kundert, Oliver; Riegel, Mariluce; Schinzel, Albert

Source: European journal of human genetics : EJHG; Apr 2015; vol. 23 (no. 4); p. 466-472

Publication Date: Apr 2015

Publication Type(s): Journal Article

PubMedID: 25005732

Abstract: The past decades have seen a remarkable shift in the demographics of childbearing in Western countries. The risk for offspring with chromosomal aneuploidies with advancing maternal age is well known, but most studies failed to demonstrate a paternal age effect. Retrospectively, we analyzed two case data sets containing parental ages from pre- and postnatal cases with trisomies 21, 13 and 18. The reference data set contains the parental ages of the general Swiss population. We dichotomized all couples into two distinct groups. In the first group, the mothers' integral age was as least as the father's age or older. We compared the frequency of cases in nine 5-year intervals of maternal age. In addition, we computed logistic regression models for the binary endpoint aneuploidy yes/no where paternal ages were incorporated as linear or quadratic, as well as smooth functions within a generalized additive model framework. We demonstrated that the proportion of younger fathers is uniformly different between cases and controls of live-born trisomy 21 as well, although not reaching significance, for fetuses over all mother's ages. Logistic regression models with different strategies to incorporate paternal ages confirmed our findings. The negative paternal age effect was also found in pre- and postnatal cases taken together with trisomies 13 and 18. The couples with younger fathers face almost twofold odds for a child with Down syndrome (DS). We estimated odds curves for parental ages. If confirmation of these findings can be achieved, the management of couples at risk needs a major correction of the risk stratification.

Database: Medline

15. Effects of increased paternal age on sperm quality, reproductive outcome and associated epigenetic risks to offspring.

Author(s): Sharma, Rakesh; Agarwal, Ashok; Rohra, Vikram K; Assidi, Mourad; Abu-Elmagd, Muhammad; Turki, Rola F

Source: Reproductive biology and endocrinology : RB&E; Apr 2015; vol. 13 ; p. 35

Publication Date: Apr 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 25928123

Abstract: Over the last decade, there has been a significant increase in average paternal age when the first child is conceived, either due to increased life expectancy, widespread use of contraception, late marriages and other factors. While the effect of maternal ageing on fertilization and reproduction is well known and several studies have shown that women over 35 years have a higher risk of infertility, pregnancy complications, spontaneous abortion, congenital anomalies, and perinatal complications. The effect of paternal age on semen quality and reproductive function is controversial for several reasons. First, there is no universal definition for advanced paternal ageing. Secondly, the literature is full of studies with conflicting results, especially for the most common parameters tested. Advancing paternal age also has been associated with increased risk of genetic disease. Our exhaustive literature review has demonstrated negative effects on sperm quality and testicular functions with increasing paternal age. Epigenetics changes, DNA mutations along with chromosomal aneuploidies have been associated with increasing paternal age. In addition to increased risk of male infertility, paternal age has also been demonstrated to impact reproductive and fertility outcomes including a decrease in IVF/ICSI success rate and increasing rate of preterm birth. Increasing paternal age has shown to increase the incidence of different types of disorders like autism, schizophrenia, bipolar disorders, and childhood leukemia in the progeny. It is thereby essential to educate the infertile couples on the disturbing links between increased paternal age and rising disorders in their offspring, to better counsel them during their reproductive years.

Database: Medline

16. Paternal age combined with maternal age influences the incidence of down syndrome

Author(s): Podder G.; Banerjee J.; Madhusnata

Source: International Journal of Pharmaceutical and Clinical Research; 2014; vol. 6 (no. 2); p. 186-188

Publication Date: 2014

Publication Type(s): Article

Abstract: Context: Genetic abnormalities, such as Down syndrome possess greater risk for Children born to older parents. Aim(s): The influence of maternal age on Down syndrome is well established, but little is known about the genetic consequences of advanced paternal age. Methods and Material: This study group included both Down syndrome patients and age, sex matched healthy controls. Result(s): In this later maternal age group, the paternal contribution to Down syndrome was more than 50%. A paternal age effect on Down syndrome was seen in association with maternal age of 35 years and above, and it was most pronounced when the maternal age was of 40 years and above. Conclusion(s): Advanced paternal age combined with maternal age influences the incidence of Down syndrome. This effect may represent a paradigm for other genetic abnormalities in children of older fathers.

Database: EMBASE

17. Paternal age and assisted reproductive outcomes in ICSI donor oocytes: is there an effect of older fathers?

Author(s): Beguería, R; García, D; Obradors, A; Poisot, F; Vassena, R; Vernaeve, V

Source: Human reproduction (Oxford, England); Oct 2014; vol. 29 (no. 10); p. 2114-2122

Publication Date: Oct 2014

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 25073975

Abstract:STUDY QUESTIONDoes paternal age affect semen quality and reproductive outcomes in oocyte donor cycles with ICSI?SUMMARY ANSWERPaternal age is associated with a decrease in sperm quality, however it does not affect either pregnancy or live birth rates in reproductive treatments when the oocytes come from donors <36 years old and ICSI is used.WHAT IS KNOWN ALREADYThe weight of evidence suggest that paternal age is associated with decreasing sperm quality, but uncertainty remains as to whether reproductive outcomes are affected. Although developed to treat severe sperm factor infertility, ICSI is gaining popularity and is often used even in the presence of mild male factor infertility.STUDY DESIGN, SIZE, DURATIONA retrospective cohort study spanning the period between February 2007 and June 2010. A total of 4887 oocyte donation cycles were included.PARTICIPANTS/MATERIALS, SETTING, METHODSFertilization was carried out by ICSI in all cycles included, and the semen sample used was from the male partner in all cases. The association of male age with semen parameters (volume, concentration, percentage of motile spermatozoa) was analyzed by multiple analysis of covariance. The association of male age with reproductive outcomes (biochemical pregnancy, miscarriage, ongoing pregnancy and live birth rate) was modeled by logistic regression, where the following covariates were introduced: donor age, recipient age, semen state (fresh versus frozen) and number of transferred embryos (3 and 2 versus 1).MAIN RESULTS AND THE ROLE OF CHANCEWe identified a significant relationship between paternal age and all sperm parameters analyzed: for every 5 years of age, sperm volume decreases

by 0.22 ml (P < 0.001), concentration increases by 3.1 million sperm/ml (P = 0.003) and percentage motile spermatozoa decreases by 1.2% (P < 0.001). No differences were found in reproductive outcomes (biochemical pregnancy, miscarriage, clinical pregnancy, ongoing pregnancy and live birth) among different male age groups.LIMITATIONS, REASONS FOR CAUTIONThe use of donor oocytes, while extremely useful in highlighting the role of male age in reproductive outcomes, limits the generalization of our results to a population of young women with older male partners. No data were available on perinatal and obstetrical outcomes of these pregnancies. Most (75%) cycles used frozen/thawed sperm samples which might have introduced a bias owing to loss of viability after thawing. ICSI was performed in all cycles to control for fertilization method; this technique could mask the natural fertilization rate of poorer sperm samples. Furthermore, we did not use stringent ICSI indications; and our data are therefore not generalizable to cases where only severe male factor is considered. However, male patients were of different racial background, thus allowing generalizing our results to a wider patient base.WIDER IMPLICATIONS OF THE FINDINGSOur study suggests that paternal age does not affect reproductive outcomes when the oocyte donor is <36 years of age, indicating that ICSI and oocyte quality can jointly overcome the lower reproductive potential of older semen.STUDY FUNDING/COMPETING INTERESTSThis study was supported in part by Fundació Privada EUGIN. The authors have no conflicts of interest to declare.

Database: Medline

18. Delayed fatherhood

Author(s): Lawson G.; Fletcher R.

Source: Journal of Family Planning and Reproductive Health Care; Oct 2014; vol. 40 (no. 4); p. 283-288

Publication Date: Oct 2014

Publication Type(s): Review

PubMedID: 24958072

Available at The journal of family planning and reproductive health care - from Unpaywall

Abstract: Birth data from developed countries indicates that the average paternal age is increasing. As the trend to older fatherhood has become established, concerns have been raised that this may be linked to adverse outcomes, such as pregnancy complications, congenital anomalies, and long-term health implications for the child. Since the sperm of older fathers may be impaired due to the general effects of ageing, their offspring may be at risk due to defects in sperm quality at conception. A literature search was performed to identify pregnancy complications, fetal anomalies and health issues for the child when the father is in an older age bracket. Evidence for impairment in the sperm and genetic material of older fathers was reviewed. With an older father, there is evidence of an increase in stillbirths and a slightly increased risk of autism, bipolar disorder and schizophrenia in the offspring later in life. The increased risk of achondroplasia has long been recognised. For the mother, there is an increased rate of Caesarean section. Investigations of other possible adverse outcomes have produced mixed findings. Further robust and longitudinal studies are needed to clarify these issues.

Database: EMBASE

19. Paternal factors in spontaneous first trimester miscarriage

Author(s): Jaleel R.; Khan A.

Source: Pakistan Journal of Medical Sciences; 2013; vol. 29 (no. 3)

Publication Date: 2013

Publication Type(s): Article

Available at Pakistan journal of medical sciences - from ProQuest (Health Research Premium) - NHS Version

Available at Pakistan journal of medical sciences - from PubMed

Abstract: Objectives: To determine whether paternal factors i.e., age, tobacco use and genital tract infection increase the risk for spontaneous first trimester miscarriage. Methodology: This case control study was conducted in the Department of Obstetrics and Gynaecology, Unit V / IV, Dow Medical College & Lyari General Hospital, Dow University of Health Sciences, Karachi, Pakistan. Duration of study was two and half years, from Nov, 2007 to Apr, 2010. Inclusion criteria were pregnant women with age 20 - 35 years irrespective of parity. Exclusion criteria were known medical illness in either partner, induced abortion and recurrent miscarriages. Studied paternal factors were age, tobacco use and genital tract infection. Data was computed using SPSS version 16. Significance of paternal factors was determined by Logistic Regression Analysis. Result(s): Total cases studied were 200, while there were 400 controls. Mean maternal age was 27.6+/-4.9 years in cases and 26.5+/-4.5 years in controls. Mean paternal age was 35.5+/-6.2 years in cases and 32.3+/-5.4 years in controls. Paternal age was >35 years in 54.5% cases and 16.8% controls. Spearman Bivariate correlation revealed paternal age > 35 years (p=0.000) and genital tract infection (p=0.043) as significant factors. Only paternal age >35 years (p=0.000) remained significant in Final Model after entering into logistic regression. Conclusion(s): Paternal age beyond 35 years was found to be significantly related to first trimester spontaneous miscarriages.

Database: EMBASE

20. Recurrent spontaneous abortion: An overview of genetic backgrounds and impact of male factors: A review

Author(s): Gaboon N.E.A.

Source: International Journal of Human Genetics; Jun 2013; vol. 13 (no. 2); p. 79-83

Publication Date: Jun 2013

Publication Type(s): Review

Available at International Journal of Human Genetics - from Free Medical Journals . com

Abstract: Genetic factors in the form of maternal or fetal single gene disorders, chromosomal abnormalities, inherited thrombophilia and other genes involved are the main causes of recurrent abortion (RA). The risk of miscarriage is highest among couples where the woman is >35 years of age and the man >40 years of age. In about 50-70% of miscarriage, a chromosome abnormality is identified in the products of conception, this chromosomal abnormality derived from one parent or the recurrence of a numerical abnormality. In about 3-5% of couples with two or three spontaneous pregnancy losses, a balanced chromosome rearrangement was found in one member of the couple. Also man's factors have an important role in RA since the man gamete contributes one-half of the genomic content to the embryo. Moreover the paternally expressed genes may have an impact on implantation, placental proliferation, and placenta quality. So any situation which leads damage of sperms DNA (e.g. varicocele) will be associated with a reduction in some fertility indices. © Kamla-Raj 2013.

Database: EMBASE

21. Predictors of trisomy 21 in the offspring of older and younger women.

Author(s): Agopian, A J; Marengo, Lisa K; Mitchell, Laura E

Source: Birth defects research. Part A, Clinical and molecular teratology; Jan 2012; vol. 94 (no. 1); p. 31-35

Publication Date: Jan 2012

Publication Type(s): Journal Article

PubMedID: 22125229

Available at Birth defects research. Part A, Clinical and molecular teratology - from Wiley Online Library

Abstract:BACKGROUNDAdvanced maternal age is the only well-established risk factor for trisomy 21, yet the majority of affected individuals are born to younger women. To identify factors associated with the risk of trisomy 21 in the offspring of younger and older women, we analyzed data for cases with trisomy 21 from the Texas Birth Defects Registry for 1999 to 2007.METHODSData were analyzed separately for younger (i.e., <35 years of age at delivery; n = 2306) and older (i.e., ≥ 35 years of age at delivery; n = 1811) women using Poisson regression.RESULTSAfter adjustment for maternal age and several other covariates, the prevalence of trisomy 21 in the offspring of women in both maternal age groups was higher in male than in female infants and in offspring of women who were Hispanic (compared with non-Hispanic white women) or who had at least one previous liveborn child compared to those with none. In the offspring of older women only, the prevalence of trisomy 21 was also significantly higher when the father was 20 to 24 years old (compared with 25 to 29 years old; adjusted prevalence ratio [aPR], 2.27; 95% confidence interval [CI], 1.47-3.49) and Hispanic (compared with non-Hispanic white; aPR, 1.34; 95% CI, 1.13-1.58) and among women with less than a high school education (compared with greater than high school).CONCLUSIONSThis study identified several factors, in addition to maternal age, that were associated with trisomy 21 risk. In general, these factors were similar for both maternal age groups, although paternal characteristics were significantly associated with risk of trisomy 21 only in offspring of older women.

Database: Medline

22. Fertility concerns for the aging male.

Author(s): Stewart, Adam F; Kim, Edward D

Source: Urology; Sep 2011; vol. 78 (no. 3); p. 496-499

Publication Date: Sep 2011

Publication Type(s): Journal Article Review

PubMedID: 21884897

Abstract: Because of many societal factors, the number of men over the age of 35 desiring to conceive children has increased over the past 40 years. The purpose of this review is to identify the mechanisms of aging on male fertility, to evaluate the genetic risk for the offspring, and to provide counseling for the older male. Most evidence suggests trends that increased paternal age has negative effects on fertility and some genetic risk for offspring, but the age at which the risk develops and the magnitude of risk are poorly defined.

Database: Medline

23. Is there a paternal age effect for aneuploidy?

Author(s): Fonseka K.G.L.; Griffin D.K.

Source: Cytogenetic and Genome Research; Apr 2011; vol. 133 (no. 2); p. 280-291

Publication Date: Apr 2011

Publication Type(s): Article

PubMedID: 21212646

Abstract: Finding a positive association between paternal age and the incidence of aneuploidy is not difficult. A cursory analysis however reveals that any association is indirect, brought about by a close correlation between paternal age and maternal age. Approaches for dissecting out the confounding age effects of the mother has led to a lively exchange among epidemiologists, with perhaps a consensus for the absence of a paternal age effect, at least for trisomy 21. Molecular studies revealed the relatively minor contribution of paternal errors to trisomy, but even research on the paternally derived trisomies alone has been inconclusive; thus studies focussed directly on the sperm heads. Human-hamster fusion assays were superseded by FISH for establishing any possible link between age and the proportion of disomic sperm in an ejaculate. Despite innumerable microscope hours however, although convincing studies suggesting an age effect for disomies 1, 9, 18 and 21 and the sex chromosomes are in the literature, others failed to notice any association for these or other chromosomes. It is biologically plausible that chromosomal non-disjunction errors should increase with age. Male reproductive hormone production, testicular morphology and semen parameters all decline slowly with age and paternal age is implicated in congenital birth defects, such as achondroplasia and Apert syndromes and also linked to compromised DNA repair mechanisms. Despite several decades of epidemiological and molecular cytogenetic studies, however, we are still not close to a definitive answer of whether or not there is a paternal age effect for aneuploidy. In this review we conclude by questioning the efficacy of FISH because of difficulties in detecting nullisomy and because of evidence that the centromeres (from which most sperm-FISH probes are derived) cluster at the nuclear centre. Array-based approaches may well supersede FISH in addressing the question of a paternal age effect; for now, however, the jury is still out.

Database: EMBASE

24. Case-control analysis of paternal age and trisomic anomalies.

Author(s): De Souza, E; Morris, J K; EUROCAT Working Group

Source: Archives of disease in childhood; Nov 2010; vol. 95 (no. 11); p. 893-897

Publication Date: Nov 2010

Publication Type(s): Research Support, Non-u.s. Gov't Multicenter Study Journal Article

PubMedID: 20584846

Abstract:OBJECTIVESTo determine whether older paternal age increases the risk of fathering a pregnancy with Patau (trisomy 13), Edwards (trisomy 18), Klinefelter (XXY) or XYY syndrome.DESIGNCase-control: cases with each of these syndromes were matched to four controls with Down syndrome from within the same congenital anomaly register and with maternal age within 6 months.SETTINGData from 22 EUROCAT congenital anomaly registers in 12 European countries.PARTICIPANTSDiagnoses with observed or (for terminations) predicted year of birth from 1980 to 2005, comprising live births, fetal deaths with gestational age ≥ 20 weeks and terminations after prenatal diagnosis of the anomaly. Data include 374 cases of Patau syndrome, 929 of Edwards syndrome, 295 of Klinefelter syndrome, 28 of XYY syndrome and 5627 controls with Down syndrome.MAIN OUTCOME MEASURESOdds ratio (OR) associated with a 10-year increase in paternal age for each anomaly was estimated using conditional logistic regression. Results were adjusted to take account of the estimated association of paternal age with Down syndrome (1.11; 95% CI 1.01 to 1.23).RESULTSThe OR for Patau syndrome was 1.10 (95% CI 0.83 to 1.45); for Edwards syndrome, 1.15 (0.96 to 1.38); for Klinefelter syndrome, 1.35 (1.02 to 1.79); and for XYY syndrome, 1.99 (0.75 to 5.26).CONCLUSIONSThere was a statistically significant increase in the odds of Klinefelter syndrome with increasing paternal age. The larger positive associations of Klinefelter and XYY syndromes with paternal age compared with Patau and Edwards syndromes are consistent with the greater percentage of these sex chromosome anomalies being of paternal origin.

Database: Medline

25. Down syndrome and paternal age, a new analysis of case-control data collected in the 1960s.

Author(s): De Souza, Elizabeth; Alberman, Eva; Morris, Joan K

Source: American journal of medical genetics. Part A; Jun 2009; vol. 149

Publication Date: Jun 2009

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 19449414

Available at American journal of medical genetics. Part A - from Wiley Online Library

Abstract: There has been a long-running debate about the association between paternal age and Down syndrome. Some studies have failed to adequately control for maternal age, and have suffered from high levels of missing paternal age, raising concerns over selection bias. This paper analyzes an anonymously case-controlled dataset with 98% complete parental age data, originally collected to investigate the association between parental exposure to radiation and Down syndrome. In our methods the cases and controls were matched on maternal age to within 6 months, and conditional logistic regression was used to estimate the odds ratio associated with a 10-year increase in paternal age. Our results showed the estimated odds ratio for a Down syndrome pregnancy associated with a 10-year increase in paternal age was 1.13, 95%CI (0.85, 1.52). There was no statistically significant evidence of an association between paternal age and Down syndrome, but the estimated association was positive. The size of the estimated effect is much smaller than the effect of maternal age.

Database: Medline

26. Ageing and genetic disorders: An experience with Down syndrome

Author(s): Kaur A.; Mahajan S.; Singh J.R.

Source: Wiener Klinische Wochenschrift; May 2009; vol. 121

Publication Date: May 2009

Publication Type(s): Conference Paper

Available at Wiener klinische Wochenschrift - from SpringerLink - Medicine

Database: EMBASE

27. Effect of maternal and paternal age on pregnancy and miscarriage rates after intrauterine insemination.

Author(s): Belloc, Stéphanie; Cohen-Bacrie, Paul; Benkhalifa, Moncef; Cohen-Bacrie, Martine; De Mouzon, Jacques; Hazout, André; Ménézo, Yves

Source: Reproductive biomedicine online; Sep 2008; vol. 17 (no. 3); p. 392-397

Publication Date: Sep 2008

Publication Type(s): Journal Article

PubMedID: 18765010

Available at Reproductive biomedicine online - from Unpaywall

Abstract: More than 17,000 intrauterine insemination (IUI) cycles were analysed retrospectively with respect to outcome according to differing aetiologies of infertility. The quantity and motility of spermatozoa in the final preparation used for insemination had a positive effect on the outcome, as classically observed in the past. It was found that advanced maternal age had a negative effect on the pregnancy rate and was associated with increased miscarriage rate. More interestingly, an exactly parallel effect was found for paternal age. The impact of increased age on necrospermia and sperm DNA structure is discussed as a probable direct cause of this paternal effect.

Database: Medline

28. The impact of male factor on recurrent pregnancy loss.

Author(s): Puscheck, Elizabeth E; Jeyendran, Rajasingam S

Source: Current opinion in obstetrics & gynecology; Jun 2007; vol. 19 (no. 3); p. 222-228

Publication Date: Jun 2007

Publication Type(s): Journal Article Review

PubMedID: 17495637

Available at Current opinion in obstetrics & gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract:PURPOSE OF REVIEWThe present paper reviews the current literature on the impact of male factor on recurrent pregnancy loss.RECENT FINDINGSMost clinicians focus their evaluation of recurrent pregnancy loss on the female, without much, if any, consideration of the other half of the couple - the male. Yet, the male contributes one-half of the genes for the embryo. Recent literature demonstrates that the male contributes to recurrent pregnancy loss due to genetic factors, semen factors or due to other factors such as age.SUMMARYRecurrent pregnancy loss results as a factor of a couple. This paper emphasizes the contribution of the male to implantation failure, miscarriage, and congenital anomalies suggested by recent literature. The current data are preliminary. With further investigation, evaluation of the male may be considered a routine part of the evaluation in the near future.

Database: Medline

29. Paternal age and birth defects: how strong is the association?

Author(s): Yang Q.; Wen S.W.; Leader A.; Chen X.K.; Lipson J.; Walker M.

Source: Human reproduction (Oxford, England); Mar 2007; vol. 22 (no. 3); p. 696-701

Publication Date: Mar 2007

Publication Type(s): Article

PubMedID: 17164268

Abstract:BACKGROUND: Although the association between maternal age and the risks of birth defects has been well studied, the evidence from population data linking paternal age with birth defects was limited and inconsistent. METHOD(S): We conducted a population-based retrospective cohort study of 5,213,248 subjects from the 1999-2000 birth registration data of the USA. Multiple logistic regressions were used to estimate the independent effect of paternal age on all birth defects and 21 specific defects groups after adjusting for potential confounding of maternal age, race, education, marital status, parity, prenatal care initiation, maternal smoking and alcohol drinking during pregnancy. RESULT(S): A total of 77,514 (1.5%) birth defects were recorded in the study cohort. The adjusted odds ratios were 1.04 (1.01, 1.06), 1.08 (1.04, 1.12), 1.08 (1.02, 1.14) and 1.15 (1.06, 1.24), respectively, for infants born to fathers 30-35, 40-44, 45-49 and over 50 years (test for trend, P = 0.0155), when compared with those infants born to fathers aged 25-29 for any birth defect. Advanced paternal age was associated with increased risks of heart defects, tracheo-oesophageal fistulaoesophageal atresia, other musculoskeletal/integumental anomalies, Down's syndrome and other chromosomal anomalies. Fathers under 25 years of age were also at increased risks of spina bifida/meningocele, microcephalus, omphalocele/gastroschisis and other musculoskeletal/integumental anomalies. CONCLUSION(S): Infants born to older fathers have a slightly increased risk of birth defects. Young paternal age is also associated with slightly increased risk of several selected birth defects in their offspring. However, given the weak association, paternal age appears to play a small role in the aetiology of birth defects.

Database: EMBASE

30. Paternal age and spontaneous abortion.

Author(s): Kleinhaus, K; Perrin, M; Friedlander, Y; Paltiel, O; Malaspina, D; Harlap, S

Source: Obstetrics and gynecology; Aug 2006; vol. 108 (no. 2); p. 369-377

Publication Date: Aug 2006

Publication Type(s): Journal Article

PubMedID: 16880308

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrics and gynecology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract:OBJECTIVETo evaluate the influence of paternal age upon spontaneous abortion.METHODSThis case-control study of 13,865 women draws on data from women's antenatal or postpartum interviews in the Jerusalem Perinatal Study, a population-based cohort derived from 92,408 births in 1964-1976. Case women (n=1,506) reported spontaneous abortion in the pregnancy preceding the interview; they were compared with women reporting live births in their previous pregnancy (n=12,359). Logistic regression was used to adjust for maternal age, maternal diabetes, maternal smoking, history of spontaneous abortions before the index pregnancy, parity at interview, and interval between the index pregnancy and the interview.RESULTSThe adjusted odds ratio for spontaneous abortion was 0.59 (95% confidence interval 0.45-0.76, P< .0001) for pregnancies conceived from fathers aged younger than 25 years compared with those from fathers aged 25-29 years. For fathers age 40 years or older the odds ratio for spontaneous abortion was 1.6 (95% confidence interval 1.2-2.0, P=.0003) when compared with the same reference group.CONCLUSIONIncreasing paternal age is significantly associated with spontaneous abortion, independent of maternal age and multiple other factors.

Database: Medline

31. Effect of paternal age on the frequency of cytogenetic abnormalities in human spermatozoa.

Author(s): Buwe, A; Guttenbach, M; Schmid, M

Source: Cytogenetic and genome research; 2005; vol. 111 (no. 3-4); p. 213-228

Publication Date: 2005

Publication Type(s): Journal Article Review

PubMedID: 16192697

Available at Cytogenetic and genome research - from ProQuest (Health Research Premium) - NHS Version

Abstract: Many surveys have been performed to find etiological relationships between pregnancy outcome and specific risk factors, such as exposure to chemicals and radiation or parental age. Advanced maternal age is a strong risk factor for trisomic pregnancies, albeit there are considerable variations among the different chromosomes. The definite incidence of the various structural and numerical chromosome aberrations in spontaneous abortions and liveborns is well known, as well as the rate of maternally and paternally derived rearrangements. Nevertheless studies have failed to assert an age-dependent risk for men fathering chromosomally abnormal children. New techniques using fluorescence in situ hybridization render it possible to analyze spermatozoa directly for numerical and, to some extent, for structural aberrations. This article compiles the findings of studies on human spermatozoa over the last few years.

Database: Medline

32. Paternal age: are the risks of infecundity and miscarriage higher when the man is aged 40 years or over?

Author(s): De La Rochebrochard, E; Thonneau, P

Source: Revue d'epidemiologie et de sante publique; Nov 2005; vol. 53

Publication Date: Nov 2005

Publication Type(s): Journal Article Review

PubMedID: 16471144

Abstract:BACKGROUNDMaternal age of 35 years or over is a well-known risk factor for human reproduction that has been extensively investigated by demographers and epidemiologists. However, the possibility of a paternal age effect has rarely been considered. We carried out review of the literature to investigate the effect of paternal age on the risks of infecundity and miscarriage.METHODSWe carried out a MEDLINE search and checked the exhaustiveness of our reference list.RESULTSWe identified 19 articles analysing the effect of paternal age. Epidemiological studies provided evidence that paternal age older than 35-40 years affects infecundity. However, the few studies based on data from assisted reproductive techniques (especially IVF with ovum donation) do not confirm this finding. All studies analysing the effect of paternal age on the risk of miscarriage showed an increased risk in men aged 35-40 years or over. Other studies have shown some evidence for a paternal age effect on late foetal deaths.CONCLUSIONThe risks of infecundity and miscarriage increase with paternal age. Two main hypotheses can be considered. First, these risks increase after the age of 35-40 years. However, a later paternal age effect (after 45-50 years) cannot be excluded. Second, due to the interaction of the ages of the two partners, the risks of infecundity and miscarriage may be higher when both partners are older (woman aged 35 years or over and man aged 40 years or over).

Database: Medline

33. Down syndrome, paternal age and education: Comparison of California and the Czech Republic

Author(s): Dzurova D.; Pikhart H.

Source: BMC Public Health; Jun 2005; vol. 5

Publication Date: Jun 2005

Publication Type(s): Article

PubMedID: 15963229

Available at BMC public health - from BioMed Central

Available at BMC public health - from SpringerLink - Medicine

Abstract: Background: The association between maternal age and risk of Down syndrome has been repeatedly shown in various populations. However, the effect of paternal age and education of parents has not been frequently studied. Comparative studies on Down syndrome are also rare. This study evaluates the epidemiological characteristics of Down syndrome in two culturally and socially contrasting population settings, in California and the Czech Republic. Method(s): The observed live birth prevalence of Down syndrome was studied among all newborns in the California counties monitored by California Birth Defects Monitoring Program from 1996 to 1997, and in the whole Czech Republic from 1994 to 1998. Logistic regression was used to analyze the data. Result(s): A total of 516,745 (California) and 475,834 (the Czech Republic) infants were included in the analysis. Among them, 593 and 251, respectively, had Down syndrome. The mean maternal age of children with Down syndrome was 32.1 years in California and 26.9 years in the Czech Republic. Children born to older mothers were at greater risk of Down syndrome in both populations. The association with paternal age was mostly explained by adjusting for maternal age, but remained significant in the Czech Republic. The association between maternal education and Down syndrome was much stronger in California than in the Czech Republic but parental age influences higher occurrence of Down syndrome both in California and in the Czech Republic. Conclusion(s): The educational gradient in California might reflect selective impact of prenatal diagnosis, elective termination, and acceptance of prenatal diagnostic measures in Californian population. © 2005 Dzurova and Pikhart; licensee BioMed Central Ltd.

Database: EMBASE

34. Influence of paternal age on the risk of spontaneous abortion.

Author(s): Slama, Rémy; Bouyer, Jean; Windham, Gayle; Fenster, Laura; Werwatz, Axel; Swan, Shanna H

Source: American journal of epidemiology; May 2005; vol. 161 (no. 9); p. 816-823

Publication Date: May 2005

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 15840613

Abstract: The frequency of chromosomal anomalies in spermatozoa appears to increase with male age. Because these anomalies play a role in the etiology of spontaneous abortion, an influence of paternal age on risk of spontaneous abortion is plausible but not established. The aim was to characterize this influence in a prospective study among 5,121 California women, who as members of a prepaid health plan were interviewed in 1990 or 1991 when they were less than 13 weeks' pregnant and who were followed until the end of pregnancy. The risk of spontaneous abortion between weeks 6 and 20 of pregnancy was studied using a Cox model adjusted for maternal age. The adjusted hazard ratio of spontaneous abortion associated with paternal age of 35 years or more, compared with less than 35 years, was 1.27 (95% confidence interval: 1.00, 1.61), with no modification by maternal age. Among women aged less than 30 years, the hazard ratio of spontaneous abortion associated with paternal age of 35 years or more was 1.56 for first trimester spontaneous abortion and 0.87 for early second trimester spontaneous abortion (test of interaction, p = 0.25). In conclusion, the risk of spontaneous abortion increased with increasing paternal age, with a suggestion that the association is stronger for first trimester losses.

Database: Medline

35. Advanced paternal age and risk of fetal death: a cohort study.

Author(s): Nybo Andersen, Anne-Marie; Hansen, Kasper Daniel; Andersen, Per Kragh; Davey Smith, George

Source: American journal of epidemiology; Dec 2004; vol. 160 (no. 12); p. 1214-1222

Publication Date: Dec 2004

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 15583374

Available at American journal of epidemiology - from Oxford Journals - Medicine

Available at American journal of epidemiology - from HighWire - Free Full Text

Available at American journal of epidemiology - from Unpaywall

Abstract:A possible detrimental paternal age effect on offspring health due to mutations of paternal origin should be reflected in an association between paternal age and fetal loss. The authors used data from a prospective study of 23,821 pregnant women recruited consecutively to the Danish National Birth Cohort from 1997 to 1999 to assess the association between paternal age and fetal death. Fathers of the pregnancies were identified by record linkage to population registers. The paternal age-related risks of fetal death and its components, early and late fetal loss, were estimated using survival analysis. Pregnancies fathered by a man aged 50 or more years (n = 124) had almost twice the risk of ending in a fetal loss compared with pregnancies with younger fathers (hazard ratio = 1.88, 95% confidence interval: 0.93, 3.82), after adjustment for maternal age, reproductive history, and maternal lifestyle during pregnancy. Various approaches to adjustment for potential residual confounding of the relation by maternal age did not affect the relative risk estimates. The paternal age-related risk of late fetal death was higher than the risk of early fetal death and started to increase from the age of 45 years. It should, however, be interpreted cautiously because of the restricted number of fetal deaths.

Database: Medline

36. Are children of older fathers at risk for genetic disorders?

Author(s): Jung A.; Schuppe H.-C.; Schill W.-B.

Source: Andrologia; Aug 2003; vol. 35 (no. 4); p. 191-199

Publication Date: Aug 2003

Publication Type(s): Review

PubMedID: 12950402

Available at Andrologia - from Wiley Online Library

Abstract: Genetic risks related to paternal age should be of interest to clinical andrologists counselling older men who wish to father a child. Theoretically, the number of (pre-meiotic) mitotic cell divisions during spermatogenesis and their remarkable increase with ageing compared with oogenesis would be in favour of genetic risks for the offspring of older men. But for numerical and structural chromosomal anomalies, such an influence of paternal age has not been found. However, in several autosomal dominant disorders affecting three specific genes (fibroblast growth factor receptor 2 and 3, RET proto-oncogene) the risk for a child to be affected increases with paternal age at time of birth. For other autosomal dominant - X chromosomal dominant or recessive disorders, the available data are sufficient to support the concept of a positive relationship between paternal age and de novo gene mutations. Studies analysing gene sequences of affected children and their parents would allow further evaluation of this topic. The impact of paternal age on disorders with a complex genetic background, however, is a matter of debate. A significant effect of paternal age

could not be shown for nonfamilial Alzheimer's disease, congenital heart defects, nonfamilial schizophrenia, acute lymphoblastic leukaemia or prostate cancer.

Database: EMBASE

37. The influence of paternal age on down syndrome.

Author(s): Fisch, Harry; Hyun, Grace; Golden, Robert; Hensle, Terry W; Olsson, Carl A; Liberson, Gary L

Source: The Journal of urology; Jun 2003; vol. 169 (no. 6); p. 2275-2278

Publication Date: Jun 2003

Publication Type(s): Journal Article

PubMedID: 12771769

Available at The Journal of urology - from Unpaywall

Abstract:PURPOSEChildren born to older parents are at greater risk for genetic abnormalities, such as Down syndrome. The influence of maternal age on Down syndrome is well established but little is known about the genetic consequences of advanced paternal age.MATERIALS AND METHODSData on the incidence of Down syndrome from 1983 to 1997 (3,419 cases) were obtained from the New York State Department of Health congenital malformations registry. Parental age was modeled as individual age groups and by a single linear covariate (drift model). The log linear chi-square test and a test of significance of different explanatory variables were used to evaluate these models to determine significance. We compared actual Down syndrome rates by maternal age with the estimated rate corrected for paternal age.RESULTSFrom 1983 to 1997 a dramatic increase in the number of infants born to parents 35 years or older was observed. During the 15-year study period there was an increase of 111% and 60% in the number of mothers and fathers 35 years old or older, respectively. There was no parental age influence on Down syndrome until age 35 years and older. A paternal age effect was seen in association with a maternal age of 35 years and older, and it was most pronounced when maternal age was 40 years and older ($p = 0.0004$). In this later maternal age group the paternal contribution to Down syndrome was 50%.CONCLUSIONSAdvanced paternal age combined with maternal age significantly influences the incidence of Down syndrome. This effect may represent a paradigm for other genetic abnormalities in children of older fathers.

Database: Medline

38. Does male age affect the risk of spontaneous abortion? An approach using semiparametric regression

Author(s): Slama R.; Boutou O.; Ducot B.; Spiral A.; Werwatz A.; Hardle W.

Source: American Journal of Epidemiology; May 2003; vol. 157 (no. 9); p. 815-824

Publication Date: May 2003

Publication Type(s): Article

PubMedID: 12727675

Available at American Journal of Epidemiology - from Oxford Journals - Medicine

Available at American Journal of Epidemiology - from HighWire - Free Full Text

Available at American Journal of Epidemiology - from Ovid (Journals @ Ovid) - Remote Access

Abstract: Couples in industrialized countries tend to delay attempting to have children, which may lower their chances of livebirth. The authors assessed the association between male age and the risk of spontaneous abortion between weeks 5 and 20 of pregnancy, controlling for female age. They interviewed by telephone a random cross-sectional population of 1,151 French women who had been pregnant between 1985 and 2000 (participation rate, 73%). A total of 12.2% of the 2,414 pregnancies resulted in spontaneous abortion. Semiparametric regression was used to define a discrete time survival model with a random effect taking into account induced abortions, in which female age was coded by a third-degree polynomial. This final model predicted that the risk (rate ratio) of spontaneous abortion was 2.13-fold higher for women age 25 years whose partner was age 35 years or older than for women age 25 years whose partner was younger than age 35 years (95% confidence interval: 1.07, 4.26). No such increased risk of spontaneous abortion with male age was estimated when the woman was age 35 years (rate ratio = 0.61, 95% confidence interval: 0.35, 1.07). Thus, increasing male age could increase the risk of spontaneous abortion when the female partner is less than 30 years of age.

Database: EMBASE

39. Down's syndrome and paternal age in Norway.

Author(s): Kazaura, Method R; Lie, Rolv T

Source: Paediatric and perinatal epidemiology; Oct 2002; vol. 16 (no. 4); p. 314-319

Publication Date: Oct 2002

Publication Type(s): Journal Article Research Support, U.s. Gov't, P.h.s.

PubMedID: 12445147

Available at Paediatric and perinatal epidemiology - from Wiley Online Library

Abstract: There is strong evidence for an effect of maternal age on the risk of Down's syndrome. An effect of paternal age has been suspected, but so far neither confirmed nor completely excluded. Large population-based data that allow detailed adjustment for maternal age are needed for a definitive analysis of the paternal age effect. We used data from the Medical Birth Registry of Norway recorded from 1967 to 1998. A total of 1738852 children were included in the analysis. A total of 10.3 per 10000 newborns had Down's syndrome. The data were fitted to logistic regression models with careful control for maternal age, birth calendar year and place of birth. When maternal age was adjusted for using categories of 5-year intervals, residual confounding still resulted in a strong effect of paternal age. However, when the shape of the effect of maternal age was well captured by the model, the estimated effect of paternal age was weak (1.11-fold increased risk per 10 years of paternal age, 95% CI of odds ratio 0.99, 1.22) and not statistically significant.

Database: Medline

40. Paternal age and maternal age are risk factors for miscarriage; results of a multicentre European study.

Author(s): de la Rochebrochard, Elise; Thonneau, Patrick

Source: Human reproduction (Oxford, England); Jun 2002; vol. 17 (no. 6); p. 1649-1656

Publication Date: Jun 2002

Publication Type(s): Research Support, Non-u.s. Gov't Multicenter Study Journal Article

PubMedID: 12042293

Abstract:BACKGROUNDIt is well known that miscarriage risk increases with age. However, studies usually investigate only maternal age effects. We investigated both maternal age and paternal age effects on miscarriage risk to provide insight into this frequent reproductive failure.METHODSThe last planned pregnancies (n = 3174) that ended in a birth or miscarriage were analysed in a retrospective population-based study on women aged 25-44 years in Denmark, Germany, Italy and Spain. Maternal and paternal ages were analysed together, using a single variable 'couple age' in a multivariate logistic regression analysis, with couples composed of a woman and a man both aged 20-29 years forming the reference group.RESULTSAfter adjustment for various factors (e.g. reproductive history, country), we found that the risk of miscarriage was higher if the woman was aged > or = 35 years, as has already been reported in a number of studies. However, the increase in risk was much greater for couples composed of a woman aged > or = 35 years and of a man aged > or = 40 years. Potential source of bias (especially 'reproductive compensation') are discussed.CONCLUSIONSThe risk of an adverse pregnancy outcome is highest if both partners are advanced in age.

Database: Medline

41. Paternal age and the risk of birth defects in offspring.

Author(s): McIntosh, G C; Olshan, A F; Baird, P A

Source: Epidemiology (Cambridge, Mass.); May 1995; vol. 6 (no. 3); p. 282-288

Publication Date: May 1995

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 7619937

Abstract: Previous studies have shown that advanced paternal age is associated with an increase in new dominant mutations that may result in some rare congenital anomalies or syndromes in the offspring. Nevertheless, few epidemiologic studies have evaluated the effect of paternal age on the risk of more common birth defects. We examined data from the British Columbia Health Surveillance Registry, which included a total of 9,660 cases of birth defects (22 specific defect groups). We chose matched controls from the birth files of British Columbia (1952-1973). With the exception of an unusual change in direction in the 45-49 years age category, we found a general pattern of increasing relative risk estimates (adjusted for maternal age and other factors) with increasing paternal age for neural tube defects, congenital cataracts, reduction defects of the upper limb, and Down syndrome. For example, the adjusted relative risk estimates for neural tube defects in the offspring were 1.2 (for fathers age 30-34 years relative to 25-29 years); 1.3 (35-39); 1.6 (40-44); 0.6 (45-49); and 2.3 (men 50 years and older). Men under 20 years of age were also at increased risk for fathering children with birth defects such as neural tube defects, hypospadias, cystic kidney, and Down syndrome. We hypothesize that among certain commonly observed birth defects a subgroup of cases may be due to new, unrecognized dominant mutations.

Database: Medline

42. Paternal age as a risk factor for Down syndrome.

Author(s): de Michelena, M I; Burstein, E; Lama, J R; Vásquez, J C

Source: American journal of medical genetics; Mar 1993; vol. 45 (no. 6); p. 679-682

Publication Date: Mar 1993

Publication Type(s): Journal Article

PubMedID: 8456845

Abstract: Although the effect of maternal age as a risk factor for Down syndrome (DS) is well known, the role of paternal age in the cause of DS has not been clearly established. To investigate this phenomenon we conducted a case-control study between July 1989 and February 1990. The cases were 318 children and teenagers with DS studied at the Specialized Educational Institutions of Lima City, Perú. They were paired with 1,196 control individuals that were selected from the birth records of 2 general hospitals of the city. For each case we tried to obtain 4 controls, paired by their date of birth, sex, and maternal age. The means of paternal age in the 2 groups were compared, first globally and then by groups of maternal age (39 years). None of the comparisons gave a statistically significant difference between the 2 groups, using either the Student t-test or the Mann-Whitney U-test. The results obtained in this study give no evidence that paternal age can be considered a risk factor for the conception of a child with DS.

Database: Medline

43. Paternal age and trisomy among spontaneous abortions.

Author(s): Hatch, M; Kline, J; Levin, B; Hutzler, M; Warburton, D

Source: Human genetics; Aug 1990; vol. 85 (no. 3); p. 355-361

Publication Date: Aug 1990

Publication Type(s): Journal Article Research Support, U.s. Gov't, P.h.s.

PubMedID: 2394449

Abstract: The relationship of paternal age to specific types of trisomy and to chromosomally normal loss was investigated in data drawn from a case-control study of spontaneous abortions. Differences in paternal age between karyotype groups and controls delivering after 28 weeks gestation were tested using an urn model analysis which adjusted, by regression, for maternal age and, by stratification, for the effects of design variables (payment status, phase of study) and demographic factors (language, ethnicity). The magnitude of paternal age differences was estimated using least squares regression analysis. For chromosomally normal cases there was no association with paternal age. Among the fourteen trisomy categories examined, four (7, 9, 18, 21) showed increased paternal age (greater than or equal to 1 year above expectation), three (13, 20, 22) showed decreased paternal age and the rest, including the most common, trisomy 16, showed negligible differences. Only the association with trisomy 22 was statistically significant (P = 0.012), with a predicted reduction in paternal age of 2.1 years (95% CI -4.9, -0.5 years). This association did not vary with maternal age, payment status, phase of study, language or ethnicity. Because previous observations are extensive, the relation of paternal age to trisomy 21 was examined further. The overall association was not significant (beta = 0.8 years; 95% CI -0.8, 2.4 years). Moreover, there was evidence that the magnitude and direction of paternal age associations vary significantly within the sample, although not between subgroups defined on the basis of payment, phase of study, language or ethnicity. With respect to maternal age, the trend is towards a greater paternal age difference for trisomy 21 losses in younger women (P = 0.058). Given the number of tests performed, the finding for trisomy 22 and reduced paternal age could be due to chance. Among trisomy types, the direction of paternal age associations was not consistent for chromosomes grouped according to characteristics that might relate to the probability of nondisjunction, such as size, arm ratio, or nucleolar organizer region content, or to the potential viability of the trisomy. Thus, neither on statistical nor biological grounds do the data provide compelling evidence of paternal age effects on the trisomies found among spontaneous abortions, or on chromosomally normal losses.

Database: Medline

44. A search for a paternal-age effect upon cases of 47, +21 in which the extra chromosome is of paternal origin.

Author(s): Hook, E B; Regal, R R

Source: American journal of human genetics; Mar 1984; vol. 36 (no. 2); p. 413-421

Publication Date: Mar 1984

Publication Type(s): Comparative Study Journal Article

PubMedID: 6231859

Available at American journal of human genetics - from PubMed

Abstract: If there is a paternal-age effect for 47, +21, it would appear most likely to be present primarily, if not exclusively, in cases in which the extra chromosome is of paternal origin. To search for such an effect, data were reviewed from seven series reporting at least four cases of 47, +21 of paternal origin. The mean of the paternal age-maternal-age difference of such cases (dp) in each series was compared with the mean of the paternal-age differences of cases in the same series that were of maternal origin (dm). If the difference between these (dp - dm or delta) is greater than zero, then this would imply a positive paternal-age effect among cases of paternal origin, at least compared to those of maternal origin. In the seven series, the values of delta ranged from -2.2 years to +3.4 years, and there was no evidence in these comparisons for any consistent trend. A second analysis controlled for any effect of maternal-age variation upon this difference. Each case of paternal origin was matched with a case of maternal origin in the same series that was of the same maternal age. Of 60 cases of paternal origin, exact matches were found for 38. In these 38, the mean value of the difference in parental ages, dp - dm or delta, was negative, about -1.1 (+/- 5.1 years). The difference was highest for the nine cases of paternal origin in which the extra chromosome resulted from presumptive second-division non-disjunction, -1.8 (+/- 3.8 years).(ABSTRACT TRUNCATED AT 250 WORDS)

Database: Medline

45. An analysis for paternal-age effect in Ohio's Down syndrome births, 1970-1980.

Author(s): Roecker, G O; Huether, C A

Source: American journal of human genetics; Nov 1983; vol. 35 (no. 6); p. 1297-1306

Publication Date: Nov 1983

Publication Type(s): Research Support, Non-u.s. Gov't Comparative Study Journal Article

PubMedID: 6228138

Available at American journal of human genetics - from PubMed

Abstract: The purpose of this study was to analyze Down syndrome (DS) births during 1970-1980 in the State of Ohio for a paternal-age effect independent of maternal age. Birth certificates and chromosome analysis records were used to ascertain 1,244 white DS births, which by capture-recapture methodology were estimated to comprise two-thirds of all white DS births in Ohio for this period. The control data consisted of 1,667,210 white live births in Ohio during the same period. One method of statistical analysis was a case-control comparison, which for each single-year maternal age compares the mean paternal age for controls with each observed DS paternal age. No statistically significant paternal-age effect was found in nine of the 11 years. For two of the years, and for all years combined, the DS fathers were significantly younger than the fathers of controls. When the data were subdivided according to ascertainment, one subpopulation--those DS individuals obtained from birth certificates alone--also showed a statistically significant negative paternal-age effect. The Mantel-Haenszel test was also applied to these data. Assuming no paternal-age effect, a lower rate of DS births than expected was found at paternal ages greater than or equal

to 40, but not at greater than or equal to 45, greater than or equal to 50, or greater than or equal to 55. These same methods were used to test for a maternal-age effect. In each of the 11 years and over all 11 years combined, a strong and statistically significant positive maternal-age effect was detected.

Database: Medline

46. Paternal age and Down's syndrome diagnosed prenatally: no association in French data.

Author(s): Roth, M P; Stoll, C; Taillemite, J L; Girard, S; Boué, A

Source: Prenatal diagnosis; Oct 1983; vol. 3 (no. 4); p. 327-335

Publication Date: Oct 1983

Publication Type(s): Journal Article

PubMedID: 6228786

Abstract: An investigation of a paternal age effect independent of maternal age was undertaken for 118 trisomy 21 cases diagnosed prenatally in 6656 amniocenteses. The mean of the difference delta in paternal age of Down's syndrome cases compared to those with normal genotypes after controlling for maternal age was +0.46 with a 95 per cent confidence interval of -0.84 to +1.76. This revealed no evidence for a paternal age effect. Multiple applications of the Mantel-Haenszel test revealed no statistically significant evidence for a paternal age effect independent of maternal age. These results are in agreement with those of Hook and Cross (1982b) but not with claims of Stene et al. (1981), of a strong paternal age effect detected in studies on prenatal diagnosis. The hypothesis suggested by Hook and Cross (1982a) that there is a rather weak paternal age effect independent of maternal age in most if not all populations cannot be excluded. If temporal or geographic factors account for the differences in studies on paternal age effect, extrapolation to other time periods or populations cannot be done.

Database: Medline

47. Paternal age and Down's syndrome genotypes diagnosed prenatally: No association in New York State data

Author(s): Hook E.B.; Cross P.K.

Source: Human Genetics; 1982; vol. 62 (no. 2); p. 167-174

Publication Date: 1982

Publication Type(s): Article

PubMedID: 6219060

Abstract: An investigation of a paternal age effect independent of maternal age was undertaken for 98 cases of Down's syndrome genotypes diagnosed prenatally compared to 10,329 fetuses with normal genotype diagnosed prenatally in data reported to the New York State Chromosome Registry. The mean of the difference (delta) in paternal age of cases compared to those with normal genotypes after controlling for maternal age, was slightly negative, -0.27 with a 95% confidence interval of -1.59 to +1.06. A regression analysis was also done in which the data were first fit to an equation of the type lny=(bx+c) and then to the equation lny=(bx+dz+c) where y=rate of Down's syndrome, x=maternal age, z=paternal age, and b, d, and c are parameters. This also revealed no evidence for a paternal age effect. The value of d (the paternal age coefficient) was in fact slightly negative, -0.0058, with an asymptotic 95% confidence interval of -0.0379 to +0.0263. Lastly, multiple applications of the Mantel-Haenszel test considering various boundaries in paternal age also revealed no statistically significant evidence for a paternal age effect detected in studies at prenatal diagnoses. Five different hypotheses are suggested which may account for discrepancies among studies to date in findings on paternal age effects for Down's syndrome: (i) there are temporal, geographic, or ethnic variations in paternal age effects, (ii) there is no paternal age effect and statistical fluctuation accounts for all trends to date; (iii) methodologic artifacts have obscured a paternal age effect in some studies which did not find a positive outcome; (iv) methodologic artifacts are responsible for the positive results in some studies to date; (v) there is a rather weak paternal age effect independent of maternal age in most if not all populations, but because of statistical fluctuation the results are significant only in some data sets. The results of all data sets to date which we have been able to analyze by one year intervals are consistent with a mean delta of +0.04 to +0.48 and in the value of d (the paternal age coefficient) of +0.006 to +0.017, and it appears the fifth hypothesis cannot be excluded. Projections based on this assumption are presented.

Database: EMBASE

48. Paternal age and Down syndrome

Author(s): Klingberg M.A.; Chen R.; Papier C.M.

Source: Congenital Anomalies; 1982; vol. 22 (no. 1); p. 1-6

Publication Date: 1982

Abstract: The association between paternal age (independent of maternal age), and Down syndrome (DS) was studied in a series of 36,011 consecutive births at Kaplan Hospital, Israel during the 11-year period (1966-1976). There were 43 DS cases in this series. The data were classed by strata of maternal age such that within each stratum, the increased risk associated with maternal age was about two-fold. Each stratum was divided into two paternal age groups - 'young' and 'aged'. 'Young' fathers were defined as those whose age did not exceed the upper limit of the mother's age stratum; 'aged' fathers, those whose aged did exceed the upper limit of the mother's age stratum. The differences between corresponding rates of DS newborns of aged and young fathers over all strata were found significant at the 5% level using the Mantel-Haenszel chi-square test with one degree of freedom. Considering the relatively small gap between median age for the corresponding paternal groups (i.e., within the same stratum), the maternal age effect does not seem to be the sole

factor responsible for the observed differences in rates of DS between corresponding paternal age groups. Difficulties generally associated with elucidating paternal age effect relative to that of maternal age are also discussed.

Database: EMBASE

49. Paternal age and Down's syndrome: data from prenatal diagnoses (DFG).

Author(s): Stene, J; Stene, E; Stengel-Rutkowski, S; Murken, J D

Source: Human genetics; 1981; vol. 59 (no. 2); p. 119-124

Publication Date: 1981

Publication Type(s): Journal Article

PubMedID: 6459986

Abstract: From prenatal diagnosis data obtained on mothers aged 35 years and above in the Federal Republic of Germany (DFG data), older fathers are demonstrated to have an increased risk of having trisomy 21 offspring. For paternal ages of 41 years upward, the age effect is quite strong. The risk for a fetus to have any de novo chromosomal aberration increases more with advancing paternal age for older mothers than for younger ones. Thus the ages of both parents have to be taken into account as an indication for prenatal diagnosis. Risk figures for trisomy 21 and for any de novo chromosomal aberration are given, together with preliminary recommendations for prenatal diagnosis for different combinations of parental ages.

Database: Medline

50. Genetic disease in the offspring of older fathers.

Author(s): Friedman, J M

Source: Obstetrics and gynecology; Jun 1981; vol. 57 (no. 6); p. 745-749

Publication Date: Jun 1981

Publication Type(s): Journal Article

PubMedID: 7231827

Abstract: Autosomal dominant genetic diseases may result from the transmission of a trait by a carrier parent or from gene mutation in one of the gametes from which the child develops. The mean age of fathers of affected persons has been found to be greater than expected for several autosomal dominant diseases due to new mutations. To assess the clinical importance of this observation, the relative and absolute frequencies of offspring with autosomal dominant diseases due to mutation in the sperm from fathers of various ages have been calculated. The relative frequency of new autosomal dominant mutations in children increases logarithmically with paternal age during the usual years of fatherhood. The absolute frequency of autosomal dominant disease due to new mutations among the offspring of fathers who are 40 years of age or older is estimated to be at least 0.3 to 0.5%. This risk is many times greater than that for children of young fathers and is similar in magnitude to the risk of Down syndrome among the offspring of 35- to 40-year-old mothers. Thus, it is good public health policy to recommend that both men and women complete their family a before age 40, if possible.

Database: Medline

51. Down syndrome associated with father's age in Norway.

Author(s): Erickson, J D; Bjerkedal, T O

Source: Journal of medical genetics; Feb 1981; vol. 18 (no. 1); p. 22-28

Publication Date: Feb 1981

Publication Type(s): Journal Article

PubMedID: 6454784

Available at Journal of medical genetics - from BMJ Journals - NHS

Available at Journal of medical genetics - from Europe PubMed Central - Open Access

Available at Journal of medical genetics - from HighWire - Free Full Text

Available at Journal of medical genetics - from PubMed

Available at Journal of medical genetics - from Unpaywall

Abstract: Records of births in Norway in 1967 to 1978 were examined for evidence of an increased risk of Down syndrome associated with older paternal age. From among some 685 000 total births with known maternal and paternal age, 693 cases of Down syndrome were reported to the Medical Birth Registry of Norway. The effect of paternal age was assessed by classifying fathers as young and old on the basis of several definitions. The effect of maternal age was removed by stratifying the data on single years of mothers' age. When fathers were considered young if they were less than or equal to 49 and old if they were less than or equal to 50, the analysis yielded a statistic for the test of a one-sided hypothesis which was significant at the 0.05 level. There appears to be an increase risk (perhaps 20 to 30%) of Down syndrome associated with older fathers, independent of maternal age effect. If this increase does in fact exist, it is much smaller than the increases in risk associated with advancing maternal age, and because older men contribute a relatively small proportion of total births their contribution to the communal burden of Down syndrome is quite small. However, the finding is of aetiological interest and is the first indication of a significant paternal age effect where control for maternal age has been stringent.

Database: Medline

52. Paternal age and Down syndrome in British Columbia.

Author(s): Hook, E B; Cross, P K; Lamson, S H; Regal, R R; Baird, P A; Uh, S H

Source: American journal of human genetics; Jan 1981; vol. 33 (no. 1); p. 123-128

Publication Date: Jan 1981

Publication Type(s): Journal Article

PubMedID: 6451171

Available at American journal of human genetics - from PubMed

Abstract: Among Down syndrome cases born in 1964--1976 reported to the British Columbia Registry for Handicapped Children, the mean parental age was about half a year greater than in the entire population of live births after controlling for maternal age, a difference significant at the .05 level. After adjustment for maternal age, a regression analysis was consistent with an increase of 1.024-fold for each year of paternal age. Among Down syndrome cases in 1952--1963, however, for which ascertainment appears likely to be less complete, there was no evidence for a significant paternal age effect. The reasons for the variation between the two groups investigated here and the heterogeneity in results among studies of other populations are discussed.

Database: Medline

53. A search for evidence for a paternal age effect independent of a maternal age effect in birth certificate reports of Down's syndrome in New York state.

Author(s): Regal, R R; Cross, P K; Lamson, S H; Hook, E B

Source: American journal of epidemiology; Nov 1980; vol. 112 (no. 5); p. 650-655

Publication Date: Nov 1980

Publication Type(s): Journal Article

PubMedID: 6449148

Abstract: The discovery that in 20% to 30% of Down's syndrome cases the extra chromosome is of paternal origin, and the recent independent report of two groups that maternal age-specific rates are two-fold greater for livebirths to couples in which the father is aged 55 years and over prompted this investigation. Analyses were of coded birth certificate reports of Down's syndrome in Upstate New York residents in the years 1963-1974. The expected numbers of cases, on the assumption of no paternal age effect, were determined at each paternal age interval (and at each paternal age minus maternal age interval) adjusting for an effect of maternal age; these were compared with observed values. There was a slightly lower number of observed than expected cases for fathers aged 55 years and over (ratio = 0.76), and the results exclude with 95% confidence an increase of 1.5-fold or greater in rates in this group after correction for maternal age. There was, moreover, no overall evidence for any trend to increasing rates with paternal age. Regression analyses in which the data were first fit to functions of maternal age and subsequently terms involving paternal age were introduced also revealed no evidence that paternal age made a significant independent contribution to the observed rates in contrast to the conclusion of earlier positive reports.

Database: Medline

54. Paternal age and Down syndrome.

Author(s): Erickson, J D

Source: American journal of human genetics; Jul 1979; vol. 31 (no. 4); p. 489-497

Publication Date: Jul 1979

Publication Type(s): Journal Article

PubMedID: 158308

Abstract: The frequency of Down syndrome (DS) in infants of older fathers has been examined in two sets of data. The effect of maternal age was controlled by single years of age. Lack of tight control has been an important weakness of other studies on this subject. Data obtained in metropolitan Atlanta by an intensive case-ascertainment program showed no overall excess of DS infants born to older fathers. Nor was there evidence of such an effect in recent birth certificate data made available by the National Center for Health Statistics. The Atlanta data suggest an increased number of DS infants born to older fathers who had children by women less than or equal to 34 years. However, there was a small deficiency of DS infants born to older fathers by women greater than or equal to 35 years. The possibility of a paternal-age effect remains open, but the available data suggest that, if it exists, it is quite small.

Database: Medline

55. Reexamination of paternal age effect in Down's syndrome.

Author(s): Matsunaga, E; Tonomura, A; Oishi, H; Kikuchi, Y

Source: Human genetics; Feb 1978; vol. 40 (no. 3); p. 259-268

Publication Date: Feb 1978

Publication Type(s): Journal Article

PubMedID: 147234

Abstract: Paternal age distribution for 1279 cases of Down's syndrome born in 1952--1968 was compared with the corresponding distribution for the general population, corrected for the maternal age as well as for the year of birth of the patients. Although there was no difference in the mean paternal age, the two distributions differed significantly, largely due to the excess of fathers aged 55 years and over and to the deficit of those aged 40--44 years in the patients born to mothers aged 30 years and over. The overall pattern of the relative incidence of Down's syndrome with advancing paternal age, with maternal age controlled, seems consistent with the hypothesis proposed by Stene et al. (1977). It increased from 0.8 for fathers aged 20--24 years slowly up to 1.2 for those aged 45--49 years, though with an intermediate drop to 0.8 at the age of 40--44 years, and then sharply to 2.4 for those aged 55 years and over. This rising pattern of the relative incidence with paternal age was essentially the same for the patients born in 1952--1960 and for those born in 1961--1968, although the slope was less steep in the latter than in the former group.

Database: Medline

56. Paternal age effect in Down's syndrome.

Author(s): Stene, J; Fischer, G; Stene, E; Mikkelsen, M; Petersen, E

Source: Annals of human genetics; Jan 1977; vol. 40 (no. 3); p. 299-306

Publication Date: Jan 1977

Publication Type(s): Journal Article

PubMedID: 139837

Abstract: Increasing incidence of Down's syndrome with advancing paternal age for given maternal age has been demonstrated. Comparisons are made between an almost complete Down's syndrome sample from the Copenhagen Metropolitan Area and a randomly selected sample of births from the same area and the same time period. Men above 55 years have a significantly increased risk of getting children with Down's syndrome.

Database: Medline

Strategy 791449

#	Database	Search term	Results
1	Medline	((paternal OR father) ADJ2 age).ti	437
2	Medline	exp "PATERNAL AGE"/	1298
3	Medline	(1 OR 2)	1400
4	Medline	exp "CHROMOSOME DISORDERS"/ OR exp "DOWN SYNDROME"/	68328
5	Medline	(chromosome ADJ2 (disorder* OR abnormalit*)).ti,ab	8147
6	Medline	("down* syndrome").ti,ab	14004
7	Medline	(miscarriage OR "spontaneous abortion").ti,ab	16367
8	Medline	exp "ABORTION, SPONTANEOUS"/	35450
9	Medline	(4 OR 5 OR 6 OR 7 OR 8)	121112
10	Medline	(3 AND 9)	258
11	EMBASE	((paternal OR father) ADJ2 age).ti	533
12	EMBASE	exp "PATERNAL AGE"/	2218
13	EMBASE	(11 OR 12)	2246
14	EMBASE	exp "CHROMOSOME DISORDER"/ OR exp "DOWN SYNDROME"/	52118
15	EMBASE	(miscarriage OR "spontaneous abortion").ti,ab	25832
16	EMBASE	exp "ABORTION, SPONTANEOUS"/	38117

17	EMBASE	("down* syndrome").ti,ab	27018
18	EMBASE	(chromosome ADJ2 (disorder* OR abnormalit*)).ti,ab	9580
19	EMBASE	(14 OR 15 OR 16 OR 17 OR 18)	106659
20	EMBASE	(13 AND 19)	361
21	EMBASE	20 [Languages English]	339