Prevalence of chromosomal abnormalities in phenotypically normal and fertile adult males: large-scale survey of over 10 000 sperm donor karyotypes

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BACKGROUND: Sperm donors represent an appropriate population for evaluating the frequency of chromosomal abnormalities in phenotypically normal and fertile adult males. METHODS: A large multicentric retrospective study was made within the French CECOS (Centre d’Etude et de Conservation des Oeufs et du Sperme) for collecting cytogenetic, biological and familial data in sperm donors over a 25-year period. RESULTS: As a whole, 10 202 karyotypes have been recorded. Thirty-eight karyotype aberrations (0.37%) have been diagnosed including 21 balanced chromosomal rearrangements (0.2%). These results are in agreement with those obtained in most large-scale studies performed in unselected newborns. Semen parameters were known for all men carrying an abnormal karyotype and showed normal sperm counts, suggesting that these types of chromosomal aberrations have no or poor consequences on spermatogenesis. Available familial data did not reveal any particular history of malformations, mental retardation or fetal losses. CONCLUSION: This study is the first large-scale cytogenetic study made in normal and fertile males and shows that the frequency of chromosomal aberrations is not influenced by a previous normal fertility or by an uneventful familial history when compared to that found at birth.

Key words: CECOS/chromosomal aberrations/fertile population/gamete donation/normal population

Introduction

The prevalence of chromosomal abnormalities in man has been extensively analysed during the seventies and eighties through large-scale karyotype studies performed in unselected newborns (Jacobs et al., 1974; Hamerton et al., 1975; Buckton et al., 1980; Hansteen et al., 1982; Maeda et al., 1991; Nielsen and Wohlert, 1991). On the other hand, cytogenetic studies in adults have always been performed in patients carrying various physical, physiological or psychological disabilities. To our knowledge, the prevalence of chromosome aberrations in a phenotypically normal and fertile adult male population is still a matter of question, even though it could be different from that observed in children at birth. A candidate population for investigating such prevalence is that of gamete donors.

Since 1973 in France, assisted reproductive technology (ART) using sperm donor insemination has been almost exclusively performed in a growing number of laboratories named CECOS (Centre d’Etude et de Conservation des Oeufs et du Sperme). They belong now to the French Federation of CECOS which, to date, is composed of 24 centres. Following the increasing use of IVF, CECOS centres have also been practising embryo cryopreservation and, more recently, oocyte donation. From 1973 to 2002, 15 535 men have volunteered their service as sperm donors in France, but, in a number of cases, sperm quality was not good enough to allow the donation process to continue. During this period, 9302 sperm samples have been successfully used for artificial insemination, leading to the birth of 38 409 children. All these gamete donors have been evaluated according to the guidelines in force at the moment of their recruitment, but each of them has had an individual genetic evaluation including karyotype. As a consequence, cytogenetic data concerning a large adult and fertile male population were thought to be available over a period of nearly 30 years. For this reason, the French Federation of CECOS decided to initiate a retrospective multicentric study concerning the cytogenetics of sperm donors.

Materials and methods

In France, sperm donors are chosen from healthy volunteers who accept to give their gametes without any economic compensation. They must be part of a couple having at least one child, and the donation process is conditional to the spouse’s acceptance. They have the awareness that their name will not be communicated to recipient couples and that the identity and the number of children conceived will
remain unknown to them. Age limit for donor inclusion has changed from 50 years till the nineties to 45 years nowadays.

For this survey, a questionnaire was sent to each CECOS centre which included the following questions: (i) the year when CECOS activity was initiated, (ii) the number of donor karyotypes analysed per year and (iii) the type of chromosomal abnormalities diagnosed. Sperm donors were recorded from the beginning of donor recruitment in each CECOS to the year 2004 inclusive. All donors gave an informed consent for karyotyping at the time of the donation process.

Because chromosomal abnormalities are often associated with spermatogenic failure, the questionnaire contained queries evaluating sperm characteristics in male donors carrying an abnormal karyotype. Indeed, biological investigations in donors, such as screening for sexually transmitted diseases, cytomegalovirus or hepatitis antibodies or karyotype abnormalities, are performed only after a first evaluation of semen parameters and resistance to both freezing and thawing procedures. As a consequence, sperm counts were thought to be available for most potential donors.

Donor karyotype analysis has been performed in several cytogenetics laboratories according to CECOS centre localization. Karyotypes have been established from blood cells according to current techniques. Nearly all of them have been analysed using R or G banding. Indeed, these techniques have been introduced in cytogenetic practice at the beginning of the seventies and, except for some rare cases in the very first years of CECOS, all the karyotypes reported here have been analysed after banding labelling.

The frequency of abnormal karyotypes in gamete donors has been compared with the frequency of the same abnormalities at birth, as reported by several studies performed in unselected newborns and also using banding techniques.

Abnormal mosaic karyotypes have been recorded when more than one abnormal cell was observed.

Familial data were collected on the basis of the pedigree, which was established at the time of donor recruitment. They included the existence of malformations, mental retardation, spontaneous repeated miscarriages or fetal losses in donor families. Every donor carrying an abnormal karyotype, or presenting a pedigree, suggesting a possible inheritance of a Mendelian inherited disease, was excluded from donation or proposed for further genetic testing, like the search for heterozygote mutations in some recessive diseases. Statistical analysis was made using the chi-square test for the comparison of abnormal karyotype frequencies between gamete donor and newborn populations.

### Results

#### Number of donor karyotypes

During the first 10 years of CECOS functioning, the number of sperm donors recruited per year increased proportionally to the number of centres in operation and to the awareness of donor sperm insemination as a new and legal treatment of male infertility in the French medical community. In the eighties, this number remained stable, around 350–400 new donors per year, but then decreased progressively during the nineties to reach its lowest level in 1999–2000, when less than 200 donors were recruited annually. In total, 10 202 sperm donors with known karyotypes were collected from 21 CECOS centres for this study, over a period of 24.3 years.

Familial and biological data were not available for every donor carrying an abnormal karyotype. Nevertheless, in France, people can be eligible for gamete donation only if they have at least one healthy child.

#### Number of chromosomal abnormalities in sperm donors

Among sperm donors, 38 (0.37%) carried a constitutional chromosomal abnormality (Tables I and II) and were excluded from donation process. When classified per 10-year period, the frequency of abnormal karyotypes overtime is stable (Table I).

Structural chromosomal abnormalities were represented by 21 balanced rearrangements (0.2%) with a known risk of

### Table I. Number of karyotypes recorded per 10-year study period

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<tbody>
<tr>
<td>1 (1979)</td>
<td>23 (0)</td>
<td>115 (0)</td>
<td>141 (1)</td>
<td>279 (1)</td>
<td></td>
</tr>
<tr>
<td>2 (1973)</td>
<td>121 (0)</td>
<td>116 (0)</td>
<td>55 (0)</td>
<td>292 (0)</td>
<td></td>
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<tr>
<td>3 (1976)</td>
<td>178 (0)</td>
<td>422 (2)</td>
<td>198 (0)</td>
<td>798 (2)</td>
<td></td>
</tr>
<tr>
<td>4 (1992)</td>
<td>0</td>
<td>0</td>
<td>178 (0)</td>
<td>178 (0)</td>
<td></td>
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<td>5 (1981)</td>
<td>19 (0)</td>
<td>171 (1)</td>
<td>134 (0)</td>
<td>324 (1)</td>
<td></td>
</tr>
<tr>
<td>6 (1978)</td>
<td>99 (0)</td>
<td>273 (3)</td>
<td>153 (1)</td>
<td>525 (4)</td>
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<tr>
<td>7 (1977)</td>
<td>115 (1)</td>
<td>255 (1)</td>
<td>52 (1)</td>
<td>422 (3)</td>
<td></td>
</tr>
<tr>
<td>8 (1974)</td>
<td>291 (2)</td>
<td>366 (1)</td>
<td>260 (0)</td>
<td>917 (3)</td>
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<tr>
<td>9 (1976)</td>
<td>276 (1)</td>
<td>356 (1)</td>
<td>134 (0)</td>
<td>766 (2)</td>
<td></td>
</tr>
<tr>
<td>10 (1985)</td>
<td>0</td>
<td>101 (0)</td>
<td>158 (3)</td>
<td>259 (3)</td>
<td></td>
</tr>
<tr>
<td>11 (1974)</td>
<td>114 (0)</td>
<td>214 (0)</td>
<td>122 (1)</td>
<td>450 (1)</td>
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</tr>
<tr>
<td>12 (1998)</td>
<td>0</td>
<td>0</td>
<td>73 (0)</td>
<td>73 (0)</td>
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<tr>
<td>13 (1995)</td>
<td>0</td>
<td>0</td>
<td>427 (4)</td>
<td>427 (4)</td>
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<tr>
<td>14 (1973)</td>
<td>281 (1)</td>
<td>186 (1)</td>
<td>161 (0)</td>
<td>628 (2)</td>
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<tr>
<td>15 (1985)</td>
<td>0</td>
<td>86 (0)</td>
<td>68 (0)</td>
<td>154 (0)</td>
<td></td>
</tr>
<tr>
<td>16 (1981)</td>
<td>35 (0)</td>
<td>179 (0)</td>
<td>73 (0)</td>
<td>285 (0)</td>
<td></td>
</tr>
<tr>
<td>17 (1977)</td>
<td>258 (1)</td>
<td>691 (3)</td>
<td>558 (2)</td>
<td>1507 (6)</td>
<td></td>
</tr>
<tr>
<td>18 (1982)</td>
<td>1 (0)</td>
<td>186 (0)</td>
<td>173 (0)</td>
<td>360 (0)</td>
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</tr>
<tr>
<td>19 (1976)</td>
<td>93 (0)</td>
<td>141 (0)</td>
<td>172 (1)</td>
<td>406 (1)</td>
<td></td>
</tr>
<tr>
<td>20 (1973)</td>
<td>151 (0)</td>
<td>172 (1)</td>
<td>197 (0)</td>
<td>520 (1)</td>
<td></td>
</tr>
<tr>
<td>21 (1976)</td>
<td>239 (1)</td>
<td>259 (2)</td>
<td>134 (1)</td>
<td>632 (4)</td>
<td></td>
</tr>
</tbody>
</table>

Total 2292 (7=1/327) 4289 (16=1/268) 3621 (15=1/241) 10202 (38=1/268)

The number of abnormal karyotypes is given in brackets and is stable overtime.
chromosomal imbalance in offspring. They included seven Robertsonian t(13:14) translocations (0.068%), five reciprocal translocations (0.05%) and nine inversions (0.088%).

Semen parameters and some familial data were available for all donors carrying a balanced structural rearrangement (Table II). Donors carrying a t(13:14) translocation had normal sperm concentrations ranging from $20 \times 10^6$ to $85 \times 10^6$ per ml. The donors carrying the t(3:18), t(7:8), t(7:14) and t(13:19) translocations had respectively $10^7$, $65$, $26$ and $49 \times 10^6$ per ml in their ejaculate. The carrier of the unusual mosaic t(7;17) translocation also had a normal sperm concentration at $96 \times 10^6$ per ml. All donors carrying an inversion also had normal sperm concentrations ranging from $40$ to $242 \times 10^6$ per ml. Available familial histories did not reveal any particular history of recurrent fetal losses, malformations or mental retardation. The death of one of the inv(6) carrier’s children was due to a coma after meningitis.

Numerical chromosome abnormalities were observed in 17 donors (0.186%). They included eight cases of mosaicism (six for the X chromosome and two for the Y chromosome), five males carrying a homogenous double Y chromosome and four cases of supernumerary markers.

Chromosomal mosaicism, leading to a 47,XXY/46,XY karyotype, was found in six donors. Except for two cases of mosaicism involving respectively 25% (4/25) and nearly 30% (17/24)
of XXY cells (published by Cozzi et al., 1994), the number of abnormal cells was very low, only two, which makes the reality of these mosaics doubtful. This is in agreement with normal sperm concentrations observed in these men of 50 and 240 × 10⁶/ml. A similar proportion of abnormal cells (2/48 and 3/63) was found in two donors with a 47,XY/46,XY mosaic male whose sperm counts were respectively 74 and 100 × 10⁶/ml.

A homogenous 47,XY chromosome complement was found in five donors (0.05%), all of them being normospermic with sperm concentrations between 55 and 120 × 10⁶/ml. Other aneuploidies included four cases of supernumerary chromosomes (0.04%), two of which had been identified respectively as a derivative chromosome 15 and another one as a marker, suggesting an isochromosome Yp in mosaic with a normal 46,XY cell line. All of these donors carrying a supernumerary marker chromosome had normal sperm concentrations ranging from 24 to 240 × 10⁶/ml.

The questionnaire also revealed a number of nonpathological chromosomal variants including seven cases of fragile sites (involving chromosomes 10 [two times], 12, 13, 16, X[q27] and X[q28]), eight nonpathological pericentric inversions of chromosome 9 and five inversions of the Y chromosomes. Other chromosomal variants, such as those involving the short arm of acrocentric chromosomes were also detected but were considered as compatible with the gamete donation process and, therefore, not always recorded. A mention must be made of pericentric inversions of chromosomes 9 and Y, which were excluded during the first decade of CECOS functioning but have been accepted since 1985 and, consequently, have not been exhaustively notified since that date.

Seven miscellaneous abnormalities were also reported by centres, including various structural (i[18q], t[7;14], inv[14], chromosome breakage and centromeric heteromorphism) or numerical (+8, +18) abnormalities that were observed in a small number of cells, if not only one.

Discussion

Large-scale studies focusing on the prevalence of both balanced and unbalanced chromosomal abnormalities in humans have been realized within unselected newborn populations (Jacobs et al., 1974; Hamerton et al., 1975; Buckton et al., 1980; Hansteen et al., 1982; Maeda et al., 1991; Nielsen and Wohlert, 1991). On the contrary, the frequency of chromosomal aberrations in adults has been established only in cases of couple infertility (Van Assche et al., 1996; Gekas et al., 2001; Vincent et al., 2002) or recurrent spontaneous miscarriages (Fryns and Van Buggenhout, 1998), mainly because ethical and practical reasons make large-scale cytogenetic studies in normal adults difficult to set up. As a consequence, the prevalence of chromosomal rearrangements in the phenotypically normal and fertile adult population is not yet clearly defined.

The systematic practice of gamete donor karyotyping within the French Federation of CECOS over a period of 30 years allowed us to collect 10 202 sperm donor karyotypes, and to our knowledge, this study represents the most important multicentric cytogenetic investigation made in the phenotypically normal and fertile adult male population. Data provided by single semen banks concerning the genetic screening for hereditary diseases in semen donors have always reported karyotype analysis in a very few number of potential gamete donors. Cytogenetic investigations carried out in 100 semen donors by del Mar Pérez et al. (1990) did not reveal any chromosomal abnormalities leading to donor’s exclusion and, among 361 sperm donors, Bick et al. (1998) found only one carrier of a chromosomal inversion [inv(7) (q11.2q22)] and four others who were possible mosaics because a single abnormal cell was observed among 30–50 analysed.

In our population, 38 chromosome abnormalities were found and included both balanced (translocations, inversions, fragile sites) and unbalanced (gonosomal aneuploidies and mosaics, supernumerary markers) anomalies, without visible phenotypic effect. This frequency does not differ from the mean frequency of the same types of abnormalities when data obtained from newborn surveys are taken together (P = 0.36). When taken separately, the frequency of these abnormalities does not statistically differ from that observed in 11 680, 3993 and 34 910 newborns by Jacobs et al. (1974) (P = 0.35), Buckton et al. (1980) (P = 0.92) and Nielsen and Wohlert (1991) (P = 0.58), respectively. The difference is, however, significant when comparing our results to those obtained by Hamerton et al. (1975) (P = 0.04), Hansteen et al. (1982) (P = 0.03) and Maeda et al. (1991) (P = 0.02) in 13 939, 1830 and 14 835 children at birth, respectively.

All these studies were performed using banding techniques but only after standard cytogenetic techniques, as was the case in our survey. For more than 30 years, these methods have remained a powerful tool for the diagnosis of most chromosomal abnormalities, and this explains why the frequency of aberrations found in our survey has been stable overtime. Indeed, high-resolution analysis of chromosomes is usually restricted to individual chromosomal studies performed in children carrying an abnormal phenotype including mental retardation, multiple malformations or dysmorphic features. To our knowledge, no large cytogenetic survey has been made in unselected newborns using high-resolution methods or molecular cytogenetic techniques such as fluorescence in-situ hybridization (FISH). Moreover, new methods such as comparative genomic hybridization (CGH) or CGH-array, which offer a considerable progress in chromosome analysis resolution, cannot detect balanced rearrangements in karyotype and, therefore, are not suitable for large-scale studies dealing with the diagnosis of both balanced and unbalanced abnormalities. Hence, our results give the frequency of chromosomal aberrations at a standard resolution level (400–500 bands) which corresponds to the level given in the large surveys made at birth.

However, in the latter, results include both balanced and unbalanced chromosomal abnormalities and concerned, for a part, children carrying or developing subsequently abnormal phenotypes. As a consequence, a case-by-case comparison between our results and the frequency of balanced chromosomal rearrangements, or at least the frequency of karyotype abnormalities without visible phenotypic effect, in the general population at birth appears preferable (Table III).

One of the most striking results in our study is the frequency (0.068%) of the t(13;14) Robertsonian translocation which is
Comparison between frequencies of chromosomal aberrations that had a normal phenotype at birth in six large surveys and in the present study

<table>
<thead>
<tr>
<th>Authors</th>
<th>Newborn number</th>
<th>Robertsonian translocations</th>
<th>Reciprocal translocations</th>
<th>Autosomal inversions</th>
<th>47.XXY</th>
<th>Marker chromosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacobs et al. (1974)</td>
<td>11 680; 7849 males, 3831 females</td>
<td>10 (0.85) [6 t(13;14) (0.5)]</td>
<td>10 (0.85)</td>
<td>2 (0.17)</td>
<td>12 (1.5)</td>
<td>[2 mosaics (0.25)]</td>
</tr>
<tr>
<td>Hamerton et al. (1975)</td>
<td>13 939; 7176 males, 6763 females</td>
<td>13 (0.93) [10 t(13;14) (0.7)]</td>
<td>11 (0.78)</td>
<td>0</td>
<td>7 (0.9)</td>
<td>[3 mosaics (0.4)]</td>
</tr>
<tr>
<td>Buckton et al. (1980)</td>
<td>3993; 2072 males, 1921 females</td>
<td>3 (0.7) [3 t(13;14)]</td>
<td>5 (1.2) [1 t(Y;15)]</td>
<td>2 (0.5)</td>
<td>4 (1.9)</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Hamerton (1982)</td>
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<tr>
<td>Hansteen et al. (1982)</td>
<td>1830; 955 males, 875 females</td>
<td>4 (2.1) [3 t(13;14) (1.6)]</td>
<td>5 (2.7)</td>
<td>0</td>
<td>1 (1)</td>
<td>4 (2.1)</td>
</tr>
<tr>
<td>Maeda et al. (1991)</td>
<td>14 835; 7608 males, 7227 females</td>
<td>11 (0.74) [9 t(13;14) (0.6)]</td>
<td>11 (0.74)</td>
<td>2 (0.13)</td>
<td>5 (0.66)</td>
<td>[3 mosaics (0.4)]</td>
</tr>
<tr>
<td>Nielsen and Wohlrert (1991)</td>
<td>34 910; 17 860 males, 17 650 females</td>
<td>43 (1.2) [34 t(13;14) (0.97)]</td>
<td>49 (1.4)</td>
<td>12 (0.34)</td>
<td>19 (1)</td>
<td>[2 mosaics (0.1)]</td>
</tr>
<tr>
<td>total</td>
<td>81 187; 43 520 males, 37 667 females</td>
<td>84 (1) [65 t(13;14) (0.8)]</td>
<td>91 (1.1)</td>
<td>18 (0.22)</td>
<td>48 (1.1)</td>
<td>[10 mosaics (0.22)]</td>
</tr>
<tr>
<td>Present study</td>
<td>10 202</td>
<td>7 t(13;14) (0.68)</td>
<td>5 (0.5)</td>
<td>9 (0.88) [3 inv(2) (0.3)]</td>
<td>5 (0.5)</td>
<td>4 (0.35)</td>
</tr>
</tbody>
</table>

Frequencies are given per 1000 in italics/brackets.

very similar to that found in newborns (0.08%) (P = 0.84). Finding seven t(13;14) translocations in normospermic men appears surprising because this type of chromosomal rearrangement is known to be diagnosed in azoospermic or oligozoospermic males, where it can be found at a frequency of 0.4% to 0.8% (Guichaoua et al., 1993; Pandiyan and Jequier, 1996; Yoshida et al., 1997). The presence of normal sperm concentrations in t(13;14) sperm donors raises the question, how these translocations may lead to spermatogenic failure in some infertile male carriers? Different chromosomal breakpoints, with the occurrence of dicentric or monocentric Robertsonian translocations, for example, could explain phenotypic variability among carriers. However, the frequent observations, in cytogenetic laboratory practice, of both fertile and infertile men carrying the same translocation within a family, suggest that sperm production impairment is due to global interactions between the translocated chromosomes and the whole genome rather than to the molecular characteristics of the translocation itself. Curiously, even if the t(13;14) is the most common type of Robertsonian translocation, no translocation between other acrocentric chromosomes was recorded, particularly no t(14;21).

Similar observations could be made about the five donors (0.049%) carrying a reciprocal translocation. This frequency is not statistically different from that observed in newborns (0.11%) (P = 0.09). Similar to Robertsonian translocations, these rearrangements are also frequently associated with spermatogenic failures and are found in 0.3–1.2% of infertile males (Guichaoua et al., 1993; Pandiyan and Jequier, 1996; Yoshida et al., 1997) and in 1.2–1.4% of couples asking for IVF by ICSI (Meschede et al., 1998; Peschka et al., 1999; Gekas et al., 2001). Sperm concentrations were available for all translocation cases in our study and were normal in the t(3;18), t(7;8), t(7;17) and t(13;19) carriers (respectively 107, 65, 96 and 49 × 10⁹/ml) and at the lower range in the t(7;14) (26 × 10⁹/ml) one which confirms the great variability of testicular impairment in reciprocal translocation male carriers.

Autosomal inversions are the second most common type of chromosomal rearrangements after translocations and are found in 0.022% of children at birth. In our study, nine pericentric inversions were found (0.088%) which is highly significant when compared with the frequency in newborns (P = 0.0008). Three of them were likely to correspond to the frequent inv(2) nonpathological variant, although chromosomal breakpoints were specified for only two of them. Among the six remaining inversions, which represent 0.058% of our donor population, chromosome 10 was involved three times. One of these inv(10) could correspond to the inv(10) (p11.2q21.2) which is also considered as a chromosomal variant without any pathological significance (Collinson et al., 1997). Three other inversions involved chromosomes 5, 6 and 11; the last two chromosomes being implicated in, respectively, three and one cases of inversion in the large survey published by Nielsen and Wohlrert (1991). Unlike paracentric inversions, which lead frequently to infertility, pericentric inversions appear to be devoid of any consequence on spermatogenesis and, indeed, semen parameters were normal in all carriers.

Other structural chromosomal abnormalities included seven cases of fragile sites. Comparing this frequency with that in newborns is difficult because these anomalies are considered as nonpathological and depend on the technical conditions in karyotype establishment, like cell-culture medium.

Beside structural chromosomal rearrangements, several cases of weak mosaicism were found in donor karyotypes, but most of them, involving either the X chromosome or an autosome, were most likely to be due to mitotic errors arising during cell cultures. This is a well-known event in cytogenetic practice and, usually, controlling karyotypes on a subsequent blood sample enables a normal karyotype to be determined.

The most relevant type of aneuploidy reported in our study was the 47.XXY homogenous karyotypes found in five sperm donors (0.05%), which is in agreement with the frequency of this chromosomal abnormality at birth (0.087%) (P = 0.29). Because most of 47.XXY men are not usually diagnosed, the frequency observed in the population referred for karyotyping is around 0.1%. Such an estimation takes into account the fact that some 47.XXY children develop mental disorders, such as...
pervasive developmental disorders or autism (Nicolson et al., 1998; Geerts et al., 2003) and that, in adults, the 47,XXY syndrome may be associated with infertility. Indeed, for unknown reasons, a number of XYY men have spermatogenesis impairment and the frequency of this aneuploidy is around 0.2–0.3% in fertile men (Pandian and Jequier, 1996; Yoshida et al., 1997; Gekas et al., 2001). In our study, all 47,XXY donors were normospermic.

Similarly, men carrying a supernumerary marker chromosome are often phenotypically normal and fertile but their frequency is increased among infertile males (Tuerlings et al., 1998; Eggermann et al., 2002). Four sperm donors were found to carry a marker in their karyotype (0.035%), which is not different from the mean frequency at birth (0.04%) (P = 0.99). They had normal sperm concentrations, including the one carrying a supernumerary marker, suggesting an abnormal isochromosome Yp in mosaic with a normal 46,XY cell line. In this latter case, a mosaic involving both a normal Y chromosome and a Y isochromosome deleted for the entire azoospermia factor (AZF), located on the Y chromosome long arm, had no deleterious effect on spermatogenesis.

Conclusion
To our knowledge, this study is the first large-scale survey of the frequency of chromosomal abnormalities in the normal and fertile adult male population, based on the study of gamete donors. Considering the large number of karyotypes reported here, our results show that the frequency of the chromosomal aberrations found in this population are similar to the incidence of the same abnormalities at birth. Consequently, a great majority of balanced chromosome rearrangements, such as translocations or inversions, or unbalanced abnormalities but without visible phenotypic effect, like Y disomy or some supernumerary markers, are clinically undetectable and remain undiagnosed in most carriers. When found by chance at birth or during a prenatal diagnosis, these anomalies cannot be considered as a significant risk of developing subsequent problems such as infertility, recurrent spontaneous miscarriages, physical or mental disabilities.

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References

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