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TEMPORAL TRENDS IN HUMAN SEMEN PARAMETERS IN NEW ENGLAND IN THE UNITED STATES, 1989–2000

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The current study explores trends in semen parameters in New England in the United States. A retrospective review was performed of 551 semen analysis records from 1989 to 2000 at Vincent Memorial Andrology Laboratory of Massachusetts General Hospital. After age adjustment, semen pH and motility significantly increased 0.05 units/year and 2.33%/year, respectively, while sperm with normal morphology decreased 0.33%/year. Sperm concentration showed a small upward trend. The year of birth in the present study ranged from 1932 to 1981; 2% were born between 1932 and 1941, 13% between 1942 and 1951, 48% between 1952 and 1961, 36% between 1962 and 1971, and 1% were born between 1972 and 1981. There were significant positive relationships between year of birth and semen volume (0.04 mL/1-year interval increase in year of birth) and motility (0.61 percent/1-year interval increase in year of birth), as well as with sperm concentration and morphology. Overall, there were temporal and year of birth trends in several human semen parameters.

Keywords human, semen parameters, sperm count, sperm morphology, sperm motility, temporal trends

During the last four decades, the number of annual office visits for infertility in the United States has risen from 600,000 in 1968 to 2 million in the 1990s [14]. Several factors may have contributed to this rise, including increases in public awareness of infertility as a treatable condition as well as an increase in couples with infertility. Approximately 15% of couples are unable to conceive after 1 year of unprotected intercourse. A male factor is solely responsible in about 20% of infertile couples and contributory in another 30–40% [18]. Semen analysis is frequently used to evaluate male infertility. Assessment of semen quality is based on the evaluation of several parameters, including semen volume, pH, sperm concentration, motility, and morphology.

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Semen quality has declined in several geographical regions worldwide during the last 60 years [1, 2, 5, 9, 16, 17]. In a meta-analysis of 61 papers published between 1938 and 1991, Carlsen et al. [5] found a statistically significant decrease in mean sperm count and seminal volume. A Parisian study also suggested a decline in concentration, motility, and morphology between 1973 and 1992 [2]. Swan et al. [16] conducted a reanalysis of the data in Carlsen's paper, as well as a reanalysis after adding 47 studies [17]. These reanalyses confirmed the downward temporal trends in semen counts [16, 17].

However, in other studies there were no temporal downward trends in sperm counts [4, 6, 12, 13, 15, 19]. A small upward trend over time in sperm concentration, semen volume, and percent sperm with normal morphology were reported in a retrospective study of 510 healthy men in the Seattle, Washington area over a 21-year period [12]. Researchers studying men in the United States banking sperm prevasectomy found a slight but significant increase in concentration of sperm [6].

The present study was designed to evaluate temporal trends in human semen parameters in men from the New England region in the United States.

MATERIAL AND METHODS

Participants and Data Source

Patients were part of couples undergoing medical evaluation for an inability to conceive. Information was collected retrospectively on a total of 551 semen analyses performed from July 1989 to December 2000. A decision was made to include only a subsample of the clinic population over this period. The records of the first 4 patients who came to the laboratory for semen analysis each month were selected. Semen volume and pH were available on 551 records. However, only 408 records had semen analyses performed using computer-assisted semen analysis (CASA). The Massachusetts General Hospital Human Subject Committee approved this study.

Collection and Evaluation of Semen

Semen was allowed to liquefy for at least 20 min in an incubator at 37°C and was analyzed within 60 min after the sample was collected. A routine semen analysis was performed. The semen assessment included semen volume, pH, sperm concentration, sperm motility, sperm progressive motility, and sperm morphology. Fresh semen samples were analyzed for sperm concentration and motion parameters by computer-aided semen analysis (CASA, Hamilton-Thorne Integrated visual optic system (HTM-IVOS Version 10, Beverly, MA, USA)). To measure both sperm concentration and motility, aliquots of semen samples (5 μL) were placed into a prewarmed (37°C) Makler counting chamber (Sefi - Medical Instruments, Haifa, Israel). A minimum of 200 sperms from at least 4 different fields were analyzed from each specimen. Percent motile sperm was defined as WHO grade "a" sperm (rapidly progressive with a velocity of $\geq 25\,\mu m/s$ at 37°C) plus "b" grade sperm (slow/sluggish progressive with a velocity of $\geq 5\,\mu m/s$ but $< 25\,\mu m/s$) [20]. As the slide was examined from one microscopic field to another, all sperm were assessed and scored as normal or abnormal. Sperm morphology was evaluated using the strict criteria by Kruger et al. [11]. A minimum of 200 sperm was counted from two slides for each

specimen. Results were expressed as the percentage of normal sperm and percentage of normal sperm with head defects, midpiece defects, and tail defects.

Statistical Analysis

To investigate whether there was a temporal trend and year of birth relationship with semen parameters, we performed multiple regression analyses (SAS version 8.2, SAS Institute, Cary, NC, USA). For each semen parameter, a separate multiple regression was performed. Age was included as a covariate in each regression model.

RESULTS

The patients ranged in age from 20 to 61 years (mean 36.3 years, SD was 6.5 years). The average (SD) sperm concentration was 136 million/mL (142.0) with a range from 2.2 to 847 million/mL and a median of 90.9 million/mL. Sperm concentration had a skewed distribution, with the mean larger than the median. The mean and median sperm concentration was higher than expected for an infertility clinic patient population. Despite the high median, 43 (11%) subjects had less than 20 million sperm/mL. There were also 6 subjects with sperm concentration greater than 750 million/mL. The mean (SD) percent motility and percent normal morphology were 62% and 8.1%, respectively. One hundred thirty-two subjects (33%) had less than 50% motility and seventy-nine (20%) had less than 4% normal morphology. The mean (SD) semen pH was 8.2 (0.4), ranged from 6.8 to 9.5, and 21% of samples were between 7.2 and 8.0.

Semen pH increased 0.05 units/year, percent motility increased 2.33%/year and sperm with abnormal morphology increased 0.33%/year. The yearly increase in percent sperm with abnormal morphology was mostly attributed to an increase in sperm head defects, and less so by an increase in sperm tail defects. Interestingly, sperm midpiece defects decreased during the 11-year follow-up period.

In the untransformed analysis, sperm concentration did not significantly increase. However, after transformation the square root of sperm concentration increased 0.18 million/mL per year (p-value < 0.01).

To further understand the yearly trends in semen parameters, the yearly median, 25th and 75th percentiles for semen pH, sperm concentration, percent motility, and percent normal morphology were plotted (Figure 1). There is an increase in semen pH during the first 5 years of data collection and then a consistent plateau. Sperm concentration increased during years 3–5 but then decreased sharply back to the year 1 concentration, only to increase sharply in the last year of data collection (Figure 1b). Although the regression analysis suggested an upward trend in sperm concentration, there is no clear trend in either direction when the yearly medians are plotted. Percent sperm motility (Figure 1c) increased during the first 4 years of data collection and then remained elevated during the remaining years, though there was a tendency for it to decrease slightly in the later years. Percent normal morphology showed a consistent downward trend (Figure 1d).

The year of birth was a significant predictor of sperm concentration (the square root of sperm concentration increased 0.07 million per mL/1-year interval increase in year of birth), normal morphology (increased 0.09%/1-year interval), and tail defects (decreased

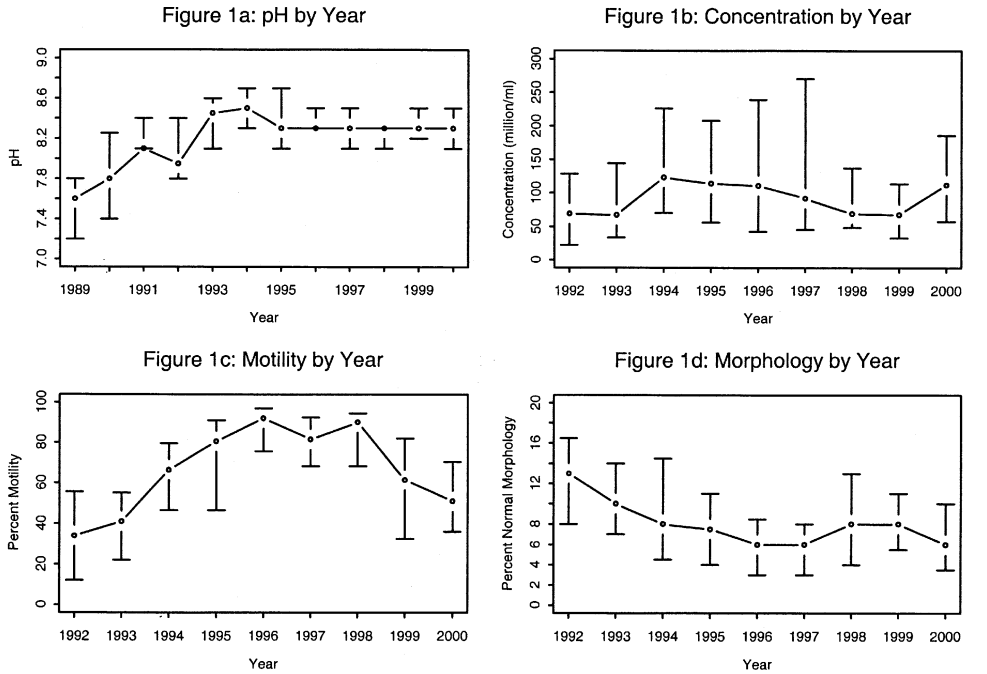

Figure 1. The median, 25th, and 75th percentiles for semen pH (a), sperm concentration (b), percent sperm motility (c), and percent normal sperm morphology by strict criteria (d) are plotted against year.

0.20%/1-year interval). In addition, semen volume increased 0.04 mL/1-year interval and progressive motility increased 0.42%/1-year interval. The unadjusted relationships between year of birth and semen parameters were similar to the analysis in which year of sample collection was adjusted for.

DISCUSSION

In the present study, the mean semen pH during the 11-year study period was 8.2, which is higher than the WHO [21] reference values of 7.2–8.0 in liquefied semen. The mean semen pH ($\pm$ SD) was 8.2 $\pm$ 0.4 with a median of 8.3 and a range from 6.8 to 9.5, with 21% of the samples between pH 7.2 and 8.0. In a Norwegian study on 207 men undergoing infertility examinations, Haugen and Grotmol [8] also found mean semen pH values above 8.0, independent of analysis method and time after ejaculation. Harraway et al. [7] also found increased mean semen pH values in a retrospective study from January 1994 to December 1998. They found a mean pH ($\pm$ SD) of 8.2 $\pm$ 0.3 with a median of 8.2. The values ranged from 7.3 to 9.5, with a pH less than 8.0 in 32% of the semen samples. These results are similar to our data and suggest that mean semen pH is higher than the WHO [21] reference values.

In the present study, there was a significant upward temporal trend in semen pH (0.05 pH units/year) and an upward trend in semen pH with year of birth (0.007 units/year). Year-by-year analysis revealed an increase in pH during the first 5 years of data collection and then a plateau. Alteration in semen pH may be indicative of accessory sex gland dysfunction [10]. Several inflammatory processes of both the prostate and seminal vesicles may alter semen pH [7]. Contrary to expectations, there was a small upward temporal trend in sperm concentration when it was entered into the models after square-root transformation. However, the upward trend was not consistent, as shown in the plot of the median yearly sperm concentration (Figure 1b). Although several studies have shown no significant change in sperm concentration [4, 13], other larger studies have shown downward temporal trends in sperm concentration.

In the present study, there was a significant upward trend in sperm concentration, after transformation, when it was regressed on year of birth. However, the evidence from other studies is inconsistent. Irvine et al. [9] studied 577 semen donors in the United Kingdom and found an association between a later year of birth and a lower sperm concentration. However, Zheng et al. [22], after adjusting for year of sample collection, failed to find an association between year of birth and sperm concentration among 8608 Danish men.

In the current study, the percentage of sperm with normal morphology significantly decreased 0.33% per year. Auger et al. [2] found that after adjusting for age and length of sexual abstinence, there was a 0.7% yearly decline in the percentage of normal sperm. Benshushan et al. [4] also found that the percentage of sperm with normal morphology decreased significantly by 1.04% per year between 1980 and 1995 in 188 young healthy medical students in Jerusalem, Israel. Their findings of a decline in sperm with normal morphology were larger than the temporal decline found in our study. Zheng et al. [26], after adjusting for year of sample collection, failed to find an association between year of birth and percent sperm with normal morphology.

The present study has several limitations that are present in retrospective temporal trend studies. This includes lack of data on potential confounders, including abstinence time and lifestyle factors. Although the direction of the bias, if any, from the above-unmeasured factors is unknown, they would most likely add random noise, thereby weakening the magnitude of the associations observed. Since the study subjects were men who were partners in infertile couples, the results of the present study may not be applicable to the general population, which includes fertile men. However, if there are temporal trends among infertility clinic populations this would be important to determine, since these men generally represent the subset of the population most vulnerable to reproductive insults. The lack of generalizability does not alter the internal validity of the study.

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