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Y-DELETIONS IN MEN WITH SEVERE OLIGOSPERMIA.
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The introduction of ICSI offered a successful treatment option for subfertile male with severe oligospermia, although the etiology of the disorder remains unclear in most cases. Recently, microdeletions in the AZFc region of the Y chromosome have been detected in men with azospermia or severe oligospermia.

In this study, we investigated the prevalence of microdeletions in the AZFc region of the Y chromosome in our ICSI population (by PCR analysis). We found 14% of the men with severe oligospermia (SCI > 5). These deletions were not found in men with no other causal factors. The results suggest that microdeletions in the AZFc region of the Y chromosome may be a contributing factor to subfertile men.

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EVALUATION OF CANDIDATE AZOSPERMIA GENES CREM, hHR6B, PMS1, AND SMCY IN CASES OF NON OBSTRUCTED AZOSPERMIA.
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INTRODUCTION AND OBJECTIVES: The increasing use of ICSI (intracytoplasmic sperm injection) for cases of male infertility underscores the importance of detecting genes involved in spermatogenesis. Evidence to date suggests that deletions within Y chromosome long arm interval 6 are associated with diffuse defects in spermatogenesis. Candidate gene distal to this region, DAZ (Deleted in Azospermia), has been identified with deletions in only 11-18% of azospermic patients. The possibility of deletions or aberrations in other genes controlling spermatogenesis exists. Recent studies involving knockout experiments of CREM (cyclic AMP-responsive Element-Modulator) and hHR6B (human homologue ubiquitin-conjugating yeast enzyme) in mice have demonstrated a variety of defects in spermatogenesis leading to either azospermic or severely oligospermic. Mutant mice deleted for a region on the Y chromosome including SMCY (a Y-specific chromosomal gene) exhibit failure of spermatogenesis.

METHODS: DNA was obtained from 56 men presenting with idiopathic infertility. cDNA to a candidate gene CREM, hHR6B, PMS1, and SMCY were obtained and a molecular probe to each created. Using Southern blot analysis, genomic DNA from each patient was then probed for each of the above candidate genes.

RESULTS: CREM, SMCY, PMS1 and hHR6B genes were identified in all 50 patients. Under stringent conditions, Southern blot analysis did not detect any large deletions resulting in differential binding patterns in any of the 34 azospermic or 16 oligospermic patients compared to normal controls.

CONCLUSIONS: Although large deletions were not observed, these data do not exclude the possibility that the above candidate genes may play a significant role in human male spermatogenesis. The possibility exists that microdeletions/mutations may contribute to gene impairment resulting in the observed phenotype.

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THE EFFECTS OF PERCOLL ON THE OPTIMIZED SPERM PENETRATION ASSAY (SPA).
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INTRODUCTION: The SPA is an important sperm function test that reveals information about sperm capacitation, acrosome reaction, membrane fusion and chromatin decondensation. At our institution, the SPA has been highly correlated with successful outcome in IUI, IVF and ICSI. Therefore, we have used extensively in sperm processing for IUI (intracytoplasmic injection), IVF and ICSI.

RESULTS: The objective of this study was to determine the effect of Percoll processing on sperm penetrating ability.

METHODS: This is a retrospective study of 253 patients out of 1200 whom underwent the optimized SPA both before and after Percoll processing from January 1993 to July 1996. 97% of patients had more than 40 million motile spermatozoa on semen analysis. The SPA result is stored by the SCI (sperm capacitation index); the SCI > 5 is normal, SCI < 5 is moderately abnormal, and SCI < 1 is severely abnormal.

RESULTS: A table summarizing the SPA results before and after Percoll processing is presented. The table shows a statistically significant improvement in the SPA results after Percoll processing.

CONCLUSIONS: Percoll processing was found to improve the SPA score in 99% of patients with mild to moderate penetration dysfunction as assessed by the SCI. It is suggested that Percoll processing can improve sperm penetration of these men in conjunction with IUI, IVF and ICSI. However, patients with severe sperm penetration abnormalities were not significantly helped by Percoll processing, suggesting that this group can only be successfully treated with ICSI.

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EFFECT OF SODIUM NITROPRUSSIDE ON SPERM MOTILITY: A DOSE-RESPONSE CURVE.
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Objective: Nitric Oxide (NO) has been shown to improve the maintenance of sperm motility in cryopreserved human sperm, as well as increase the yield of motile sperm using swim-up methods. However, an inhibition of sperm motility by NO at higher concentrations has also been reported. This suggests that NO may exert its effect on motility in a dose dependent manner. To investigate this hypothesis, we generated dose-response curves to evaluate the effects of NO on sperm motility over a wide range of concentrations using sodium nitroprusside as the NO donor.

Methods: Motile sperm obtained from two known fertile donors (two specimens each) and three infertile patients were separated on a Percoll gradient. Sodium nitroprusside was added in decreasing concentrations to the washed semen aliquots, to achieve final concentrations in the tube of 1x10^{-2} to 1x10^{-6} M. Sperm concentration in each tube was 2 million/ml. A control tube was maintained without sodium nitroprusside. Sperm motility was evaluated after two hours incubation at 37°C.

Results: Sperm motility in the control ranged from 71% to 84%. High concentrations of sodium nitroprusside (1x10^{-6} M and 1x10^{-5} M) were inhibitory to sperm motility resulting in final motility of 1% to 39%. At the concentration of 1x10^{-5} M, sperm motility returned to baseline value (i.e. control motility). Between 1x10^{-5} M and 1x10^{-4} M sodium nitroprusside, there was a trend towards enhanced motility (range: 71% to 85%).

Conclusions: The dose-response curves for both donors and patients were indentical, that is, inhibition at higher concentrations of sodium nitroprusside (1x10^{-5} M and 1x10^{-4} M) and no inhibition or mild enhancement of sperm motility at lower concentrations of sodium nitroprusside (1x10^{-6} M and 1x10^{-5} M).