

independent reviewers making a manual call on the data, there is some variability. Continued improvements in analysis of genetics results to increase consistency though use of AI and other approaches is likely prudent, especially with niPGTA.

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TRENDS IN PREIMPLANTATION GENETIC TESTING FOR DOUBLE MONOGENIC DISORDERS (PGT-M).

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BACKGROUND: Preimplantation genetic testing for monogenic disorders (PGT-M) can be performed on embryos prior to transfer when a variant or mutation is identified in a single gene. PGT-M has historically been utilized to evaluate embryos for severe, highly penetrant and childhood-onset diseases.¹ However, the use of PGT-M has significantly increased due to increased genetic testing³ and expanded indications.⁴⁻⁵

OBJECTIVE: To investigate indications, trends and outcomes when PGT-M is performed for two or more monogenic disorders simultaneously.

MATERIALS AND METHODS: This is a case series in a single university-based fertility center. All PGT-M cases involving testing for two or more genes as well as preimplantation genetic testing for aneuploidy (PGT-A) between January 2010 and October 2021 were reviewed. Genes 1, 2 and 3 were defined as genes of interest discovered in chronological order respectively. Primary outcomes included indication for presentation to fertility center, PGT-M indication, type of condition, age of condition onset and PGT-M inheritance pattern. Secondary outcomes included genetic result of transferred embryo and ongoing pregnancy rates defined as pregnancies greater than 20 weeks gestation divided by total single thawed euploid embryo transfers (STEET).

RESULTS: This study included 363 biopsied blastocysts from 49 retrievals, in 23 patients who had 24 STEET. 56%(13/23) of patients presented between 2019 and 2021, with 30%(7/23) presenting in 2021 alone. The majority initially presented for double PGT-M[44%(10/23)]. 39%(9/23) presented initially for single PGT-M, with a second gene identified later. 4%(1/23) presented for triple PGT-M. 13%(3/23) presented for infertility with no previous genetic testing. Across the 23 patients, 47 genes were tested and 34 of those were unique. The most commonly tested genes were BRCA1/2[11%(5/47)], HLA[11%(5/47)], FMR1[6%(3/47)], GJB2[6%(3/47)], MSH2[4%(2/47)] and SLC26A4[4%(2/47)]. The majority of genes tested cause childhood-onset diseases[68%(32/47)]. 23% were adult-onset and 8% were variable-onset. The majority were split between autosomal dominant (AD) [38%(18/47)] and autosomal recessive (AR)[38%(18/47)]. 13%(6/47) were X-linked and 10%(5/47) were for HLA matching. PGT-M indication for first gene identified included previous child affected[30%(7/23)], carrier screening[26%(6/23)], patient affected[22%(5/23)] and partner affected[22%(5/23)]. PGT-M indication for second gene identified included carrier screening[43%(10/23)], previous child affected[26%(6/23)], patient affected[22%(5/23)] and partner affected[9%(2/23)]. Patients underwent an average of 2.1 retrievals. 22%(11/49) of retrievals resulted in no embryos suitable for transfer requiring an average of 1.3 additional retrievals per patient. 13%(3/23) of patients had no embryos suitable for transfer. Of the 24 embryos transferred, 12/24(50%) were euploid and non-carriers, 11/24(46%) were euploid and autosomal recessive carriers of one gene and 1/24(4%) was euploid female and a pre-mutation carrier of FMR1. There were no embryos transferred that were carriers of 2 mutations. 75%(18/24) of STEET resulted in ongoing pregnancies.

CONCLUSIONS: From the preceding decade in our clinic, PGT-M for two or more genes increased by 43% in 2021. Over this time, there has been a shift towards more testing for AD over AR disorders due to an increase in BRCA1/2 testing. The majority of patients who attempt double or more PGT-M are able to obtain unaffected or autosomal recessive carrier euploid embryos with ongoing pregnancies despite requiring an often-increased number of cycles. We expect demand for multi-gene PGT-M to rise with increased and expanded utilization of preconception comprehensive genetic screening.

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REFERENCES:

1. ESHRE PGD Consortium Steering Committee. ESHRE Preimplantation Genetic Diagnosis Consortium data collection III (May 2001). *Hum Reprod.* 2002 Jan;17 (1) 233-46.
2. Besser AG, McCulloh D, McCaffrey C, Grifo JA. Trends in Preimplantation Genetic Testing for Monogenic Disorders (PGT-M). American Society for Reproductive Medicine Meeting 2021. Baltimore, MD.
3. Besser AG, Blakemore JK, Grifo JA, Mounts EL. Transfer of embryos with positive results following preimplantation genetic testing for monogenic disorders (PGT-M): Experience of two high-volume fertility clinics. *J Assist Reprod Genet.* 2019 Sep; 36 (9) 1949-1955.
4. Baruch S, Kaufman D, Hudson KL. Preimplantation genetic screening: a survey of in vitro fertilization clinics. *Fertil Steril.* 2008. May; 89 (5): 1053-1058.
5. Mounts EL, Besser AG. Genetic Counseling for preimplantation genetic testing (PGT): Practical and Ethical Challenges. In Sills E, Palermo G, editors. *Human Embryos and preimplantation genetic technologies.* Academic Press; 2019. p 43-52.

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SEMEN ANALYSIS FINDINGS FROM LARGE COHORT OF ADOLESCENTS WITH KLINEFELTER SYNDROME.

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INTRODUCTION: Klinefelter Syndrome (KS) is the most common genetic condition cause of non-obstructive azoospermia (NOA). KS also often results in decreased testicular growth and testosterone production. Because of this, exogenous testosterone therapy is commonly prescribed for KS patients to treat hypogonadism, but this may have additional impacts to future fertility potential. Current clinical practice is to have KS adolescent patients provide frequent semen samples in an effort to identify potential sperm for early cryopreservation.

OBJECTIVE: Given the limited data in this patient population, our objective was to develop a multi-institutional database to identify if frequent semen analysis evaluation is necessary and practical for fertility preservation and family planning.

MATERIALS AND METHODS: A retrospective study was performed of all adolescent KS patients seen at two tertiary male infertility clinics between 2015 and 2020. Adolescence was defined as individuals aged 10 – 19 years, as per the World Health Organization. Demographic information data including weight, height, medical comorbidities, and concurrent medications were collected. Serum hormone levels including FSH, LH, testosterone, and estrogen were collected as well as any available semen analysis data.

RESULTS: A total of 48 patients were identified with hormonal data and semen analyses. 3 (6.3%) patients had rare sperm in the ejaculate while the remaining had azoospermia (93.8%). The average serum total testosterone level of adolescent KS patients was 181 ± 216 ng/dL. FSH levels were 14.3 ± 18.8 IU/L (normal 0.3 – 10.0 IU/L) and LH levels were 7.8 ± 12.4 IU/L (normal 1.2 – 7.8 IU/L).

CONCLUSIONS: The findings from the largest retrospective cohort of this patient population imply a need to revisit counseling regarding the need for frequent semen analyses in adolescent KS patients, as the vast majority were found to be azoospermic. Even in the rare case where sperm was identified in adolescent KS patients, cryopreservation may not be feasible.

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SWIPE RIGHT ON MALE INFERTILITY: EFFECT OF CELL PHONE RADIATION ON SPERM MOTILITY.

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BACKGROUND: Over the past decade, the relationship between humans and their smartphones have been marked with stark symbiosis. The advent of Bluetooth earbuds has presumably prolonged the amount of time the cell phone resides in the trouser pockets of men. This places the smartphone and its respective radiofrequency - electromagnetic radiation (RF- EMR)

near the testicles. RF-EMR has been postulated to increase oxidative stress and induce free radical formation.

OBJECTIVE: We hypothesized that RF-EMR from cell phones has deleterious effects on sperm parameters, though these effects can be mitigated with solid mediums or distance.

MATERIALS AND METHODS: We evaluated the impact of current generation smartphone, in talk mode, as the RF-EMR source. We certified the exposure to the specimen using calibrated RF-EMR meter (validated in previous studies). Initially, we studied the impact of RF-EMR on sperm motility and viability from fertile, normozoospermic men, between the ages of 25–35 years old by exposing their semen in an *in vitro* study over an 8-hour duration. We then determined whether using a cell phone case and increasing distance from semen sample would make a difference in outcomes. Statistical differences were analyzed using paired t student test for comparisons between two sub-groups where $p < 0.05$ was set as significant.

RESULTS: At 6 hours after exposure, we identified a decrease in sperm motility and viability in samples exposed to RF-EMR as compared to those samples that were not from fertile controls. With the addition of the case, we noted a smaller impact on total sperm motility and viability ($p = 0.01$, $p = 0.01$) as compared to direct RF-EMR exposure. In fact, moving the cell phone away by 3 inches represented the best mitigation strategy to deleterious effects on sperm motility and viability. Interestingly, when the phones were turned on in the talk-mode, most detrimental effects on sperm motility were identified.

CONCLUSIONS: In this pilot study, we observe that the sperm parameters of motility and vitality are impacted with RF-EMR exposure from cell phones. Precautionary measures such as physical shields and increased distance from the scrotum dampened the effects of RF-EMR. Further *in vivo* research on the true impact of cell phone radiation on male fertility potential is warranted.

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FAILED THAW CYCLES (FTHC) AS A KEY PERFORMANCE INDICATOR (KPI): ACCOUNTING FOR THE POTENTIAL IMPACT OF PREIMPLANTATION GENETIC TESTING (PGT) ON EMBRYO SURVIVAL. Wirka KA,¹ Mahony MC,² Hayward B,¹ Collares F,¹ Modrzejewski K,¹ Macalino G,³ Byrne M,³ Catherino AB.¹ ¹EMD Serono, Inc., Rockland, MA, USA; ²Independent Scientific Affairs Consultant, Virginia Beach, VA, USA; ³Marimac Insight, Columbia, MD, USA.



BACKGROUND: The percentage of failed thaw cycles (FTHC; ie, thaw procedures that failed to produce any embryos suitable for transfer) has been suggested as a surrogate for laboratory competency in freezing/thawing procedures, thus a potential key performance indicator (KPI) for IVF laboratories. Previous analysis showed that proportion of FTHC significantly decreased in the USA between 2014 and 2019 across all ages and infertility diagnoses, while the total number of frozen embryo transfer (FET) thaw procedures increased [1]. We postulated that preimplantation genetic testing (PGT) could be one of the key drivers of FTHC improvement.

OBJECTIVE: To evaluate the impact of PGT on the proportion of FTHC over time (stratified by age) and assess whether use of PGT should be considered when evaluating FTHC as a KPI for FET cycles.

MATERIALS AND METHODS: We analyzed six years of available data (2014–2019) from the Society for Assisted Reproductive Technology (SART) database, including a total of 264,949 FET cycles, stratified by SART age groups and PGT use. Outcomes included proportion of FTHC, mean number of embryos transferred, and live birth rates (LBRs). Multivariable logistic regression was used to assess the relationships between variables. Differences in mean number of embryos transferred and LBRs over time were evaluated using a linear test of trend.

RESULTS: The proportion of FTHC significantly decreased over time across all ages, independent of PGT, except in patients aged >42 years. The number of FTHC increased with age (>42 years versus <35 years: unadjusted odds ratio=4.4; 95% CI 3.9–5.0). After adjusting for year and age, the odds of FTHC were 37% lower with PGT versus without PGT.

The effect of PGT on FTHC was more apparent in older patients. In patients aged <35 or 35–37 years, the proportion of FTHC decreased over time with ($p < 0.0001$ and $p = 0.0003$, respectively) or without PGT ($p < 0.0001$ for both; **Table**). In older age groups, the proportion of FTHC did not change significantly over time for cycles without PGT but showed significant improvement with PGT, particularly in patients aged >42 years (**Table**).

Across all ages, independent of PGT, the mean number of embryos transferred significantly decreased over time ($p < 0.0001$), while LBRs significantly increased ($p < 0.0001$). PGT effect on LBR increased over time in patients aged 38–40 ($p < 0.0001$), 41–42 ($p = 0.0026$), and >42 years ($p < 0.0001$), but no significant change was detected without PGT.

CONCLUSIONS: PGT use was associated with improved proportion of FTHC and LBR, particularly in older patients. Thawing embryos screened as euploid appears to be a significant contributor to embryo survival and clinical outcomes. Other likely contributors include the evolution of freezing criteria, procedures, and clinical/laboratory decisions that positively impact LBRs. When evaluating FTHC as a KPI for FET cycles, laboratories should consider the impact of PGT. Additional analysis stratifying by diagnosis is underway.

Table: Proportion of FTHC over time, stratified by SART age groups and PGT status

SART age groups by PGT status	FTHC ^a %, failed thaws/all thaws						p-value
	2014 (n=32381)	2015 (n=37709)	2016 (n=42244)	2017 (n=45526)	2018 (n=50363)	2019 (n=56726)	
<35 years	(n=15322)	(n=17863)	(n=19836)	(n=21104)	(n=22601)	(n=24401)	
No	1.1, 160/14,201	1.0, 160/15,515	0.8, 133/16,034	0.6, 92/15,888	0.5, 77/15,966	0.5, 84/15,891	<0.0001
Yes	1.3, 15/1121	1.0, 23/2348	0.7, 26/3802	0.5, 27/5216	0.3, 22/6635	0.3, 22/8510	<0.0001
35–37 years	(n=8085)	(n=9410)	(n=10948)	(n=11942)	(n=13393)	(n=15304)	
No	1.5, 111/7339	1.1, 85/7808	1.0, 86/8370	0.8, 62/8169	0.6, 51/8467	0.8, 67/8658	<0.0001
Yes	1.3, 10/746	1.0, 16/1602	0.5, 14/2578	0.5, 20/3773	0.5, 24/4926	0.3, 20/6646	0.0003
38–40 years	(n=5617)	(n=6465)	(n=7192)	(n=7918)	(n=8912)	(n=10551)	
No	1.6, 77/4954	1.7, 88/5143	1.6, 83/5116	1.2, 57/4879	1.2, 60/5086	1.3, 67/5289	0.0633
Yes	1.5, 10/663	0.5, 7/1322	0.9, 18/2076	0.9, 27/3039	0.6, 23/3826	0.4, 22/5262	0.0061
41–42 years	(n=1881)	(n=2325)	(n=2509)	(n=2765)	(n=3243)	(n=3747)	
No	2.6, 42/1631	1.6, 28/1792	2.0, 34/1728	1.7, 29/1659	2.3, 40/1711	1.4, 24/1716	0.0993
Yes	1.6, 4/250	0.8, 4/533	0.8, 6/781	1.3, 14/1106	1.7, 26/1532	0.6, 12/2031	0.0289
>42 years	(n=1476)	(n=1646)	(n=1759)	(n=1797)	(n=2214)	(n=2723)	
No	2.9, 38/1310	3.8, 50/1325	3.5, 45/1290	3.6, 41/1142	3.5, 47/1325	3.3, 47/1409	0.8798
Yes	6.0, 10/166	1.9, 6/321	2.3, 11/469	2.1, 14/655	1.8, 16/889	1.5, 20/1314	0.0079

PGT included PGT-A, PGT-SR, and PGT-M. P-values were obtained using Pearson's Chi-square test of significance. an in bracket represents total number of thaws.

FTHC, failed thaw cycles; PGT, **preimplantation genetic testing**; PGT-A, PGT for aneuploidies; PGT-M, PGT for monogenic/single gene defects; PGT-SR, PGT for structural chromosomal rearrangements; SART, Society for Assisted Reproductive Technology