



# *Better Sperm, Better IVF?*

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# *Disclosures*

- Nothing to Disclose



## *Topics for Discussion and Learning Objectives*

- **Discuss the AUA Guidelines update. (10 mins)**
- **Discuss At-home semen analysis. (5 mins)**
- **Review Clinical scenarios. (20-25 mins)**
- **Describe What's on the Horizon? (5 mins)**



*Live poll – Who is in the room?*

- **Reproductive endocrinology**
- **Embryology/andrology**
- **Research**
- **Industry**
- **Urology**





## *Live poll*

- **Access to reproductive urology resource**
  - Urologist in your practice
  - Male reproductive specialist in your region
  - Several reproductive urology options
  - No local option for reproductive urology/use general urologist



*Live poll – Where are your simple sperm retrievals performed?*

- **In your lab/ambulatory center?**
- **In an offsite center of the urologist's choosing?**
- **In a hospital?**
- **In the urologist's office?**



## *Live poll*

- **Do you have the ability to do fresh in-cycle TESE cases?**
  - Yes
  - No



## *AUA Guidelines Panel – Male Infertility*

- **AUA/ASRM joint venture**
- **Original guidelines 2020**
- **Amended guidelines 2024**
- **Panel of 14 experts in male infertility, 6 staff/consultants**
- **54 guidelines addressing the workup, impact of lifestyle factors, diagnosis/evaluation, imaging, and treatment of infertile male patients.**



# AUA Guidelines

Table 2: Strength of Evidence Definitions

AUA Strength of Evidence Category	GRADE Certainty Rating	Definition
A	High	<ul style="list-style-type: none"><li>• Very confident that the true effect lies close to that of the estimate of the effect</li></ul>
B	Moderate	<ul style="list-style-type: none"><li>• Moderately confident in the effect estimate</li><li>• The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</li></ul>
C	Low	<ul style="list-style-type: none"><li>• Confidence in the effect estimate is limited</li><li>• The true effect may be substantially different from the estimate of the effect</li></ul>
	Very Low	<ul style="list-style-type: none"><li>• Very little confidence in the effect estimate</li><li>• The true effect is likely to be substantially different from the estimate of effect</li></ul>



# *AUA Guidelines*

Clinical Principle	a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature
Expert Opinion	a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature





## *Level B Evidence*

- #2: Clinicians should include a reproductive history during initial evaluation of the male for fertility. (*Clinical Principle*) Clinicians should also include one or more semen analyses (SAs) during initial evaluation of the male. (*Strong Recommendation; Evidence Level: Grade B*)
- #5: Clinicians should counsel infertile males or males with abnormal semen parameters on the health risks associated with abnormal sperm production. (*Moderate Recommendation; Evidence Level: Grade B*)
- #6: For infertile males with specific, identifiable causes of male infertility, clinicians should inform the patient of relevant, associated health conditions. (*Moderate Recommendation; Evidence Level: Grade B*)



## *Level B Evidence*

- #13: Clinicians should recommend Y-chromosome microdeletion analysis for males with primary infertility and azoospermia or sperm concentration  $\leq 1$  million sperm/mL when accompanied by elevated follicle-stimulating hormone, testicular atrophy, or a diagnosis of impaired sperm production. (*Moderate Recommendation; Evidence Level: Grade B*)
- #26: Clinicians should consider surgical varicocelectomy in males attempting to conceive who have palpable varicocele(s), infertility, and abnormal semen parameters, except for azoospermic males. (*Moderate Recommendation; Evidence Level: Grade B*)
- #45: Clinicians should counsel patients that the benefits of supplements (e.g., antioxidants, vitamins) are of questionable clinical utility in treating male infertility. Existing data are inadequate to provide recommendation for specific agents to use for this purpose. (*Moderate Recommendation; Evidence Level: Grade B*)





## *Level B Evidence*

- **#46:** For males with idiopathic infertility, clinicians may consider treatment using a follicle-stimulating hormone analogue with the aim of improving sperm concentration, pregnancy rate, and live birth rate. (*Conditional Recommendation; Evidence Level: Grade B*)
- **#54:** Clinicians should inform males seeking paternity who are persistently azoospermic after gonadotoxic therapies that microdissection testicular sperm extraction is a treatment option. (*Strong Recommendation; Evidence Level: Grade B*)



# *Clinical Guidelines Breakdown by Data Strength*

- **Level**

- **A: none**
- **B: 8/54 (15%)**
- **C: 13/54 (24%)**
- **Expert Opinion: 27/54 (50%)**
- **Clinical Principle: 6/54 (11%)**



## *AUA Guidelines*

- <https://www.auanet.org/guidelines-and-quality/guidelines/male-infertility>



## *At-home test methodology*

- **Directly observed (smartphone camera and magnifying device)**
  - Yo
  - Loupe
  - ExSeed
- **Mail-away**
  - Fellow
  - Legacy
  - Reprosource
- **Indirect**
  - SpermCheck



## *At-home testing – take home points*

- **For the most part, at-home testing has a reasonable degree of accuracy**
- **Motility can be a concern, particularly for the mail-away**
- **Significantly lowers the barrier to entry for many men**
- **Reasonable first step to possibly identify male factor early in the conception pathway**
- **Does NOT replace a full laboratory based semen analysis and reproductive urology evaluation**



# *A New Age of Consumer Accessible Sperm Testing*

- **At-home testing**
- **Advanced Sperm Testing (Andrology Lab)**
  - DNA fragmentation
  - Epigenetics
  - Phosphatidylserine
  - ATP
  - Sperm sorting techniques



## *Patient #1 – “Blue Monday”*

- **34 yo data scientist with no prior fertility testing or conceptions, is engaged to be married, wants to assess his baseline fertility parameters**
  - **No medical or surgical issues, normal exam**
  - **SA #1: 3.1 mL, 65 M/mL, 49% motility, 1% morphology**
  - **SA#2: 2.6 mL, 58 M/mL, 39% motility, no normal forms seen in 300 sperm**





## *Live Poll – “Blue Monday”*

- **1) Reassure and see back PRN**
- **2) Recommend timed intercourse**
- **3) Would you skip IUI?**
- **4) IVF w ICSI**





## *Sperm morphology has changed over the decades*

- WHO 1&2 – no obvious defects (81%)
- WHO 3 – 30%
- WHO 4 & 5 – 14%/4%



# WHO 6 Semen Analysis Criteria

Table 8.3 Distribution of semen examination results from men in couples starting a pregnancy within one year of unprotected sexual intercourse leading to a natural conception. From Campbell et al. (5); fifth percentile given with variability (95% confidence interval)

	N	Centiles									
		2.5th	5th	(95% CI)	10th	25th	50th	75th	90th	95th	97.5th
Semen volume (ml)	3586	1.0	1.4	(1.3–1.5)	1.8	2.3	3.0	4.2	5.5	6.2	6.9
Sperm concentration (10 <sup>6</sup> per ml)	3587	11	16	(15–18)	22	36	66	110	166	208	254
Total sperm number (10 <sup>6</sup> per ejaculate)	3584	29	39	(35–40)	58	108	210	363	561	701	865
Total motility (PR + NP, %)	3488	35	42	(40–43)	47	55	64	73	83	90	92
Progressive motility (PR, %)	3389	24	30	(29–31)	36	45	55	63	71	77	81
Non-progressive motility (NP, %)	3387	1	1	(1–1)	2	4	8	15	26	32	38
Immotile spermatozoa (IM, %)	2800	15	20	(19–20)	23	30	37	45	53	58	65
Vitality (%)	1337	45	54	(50–56)	60	69	78	88	95	97	98
Normal forms (%)	3335	3	4	(3.9–4.0)	5	8	14	23	32	39	45



## *Sperm morphology – does it matter?*

- **Kohn et al 2018 – no impact of morphology on IUI outcomes (20 studies, 42k IUI cycles)**
- **Muthigi et al 2022 – no impact of morphology on IUI outcomes (100k+ IUI cycles)**
- **Samplaski 2019 – overview of available literature – morphology impact conflicting results, more recent ART data would suggest no impact**
- **Atmoko et al 2024 – Systematic review of 88 articles – unclear significance of isolated teratozoospermia**



## *Possible interventions for isolated morphology deficit*

- **Do nothing**
- **Varicocele repair**
- **Antioxidants**
  - **CoEnzyme Q10**
  - **L-Carnitine**
- **IUI**
- **IVF (+/- ICSI)**



## *Patient #2 – “Friday I’m in Love”*

- **38 yo with 14 months TTC, partner is 38 yo.**
  - **No gynecologic issues, 28-30 d cycle**
  - **She works for World Bank and is in Kenya for 2 weeks every other month**
  - **They would like 2 children**
  - **Known varicocele since age 14, one prior VIP 10 yrs ago w different partner**
  - **SA: 3.7 mL, 128 M/mL, 45% motility, 3% morphology**
  - **SCSA 38% fragmentation**



## *Live Poll – Next step*

- **Continue more timed intercourse**
- **IUI with fresh/cryo sperm**
- **IVF with ejaculated sperm**
- **IVF with TESE sperm**





## *Overview of Sperm DNA fragmentation*

- **Oxidative stress can affect sperm in different ways**
- **Apoptosis**
- **Sub-lethal oxidative stress can disrupt varying aspects of cellular function, including DNA packaging and replication**
- **Incomplete/inadequate DNA packaging can lead to more exposed DNA to OS and subsequent DNA damage as the sperm transit through the male reproductive tract**



## *Sperm DNA Fragmentation*

- **High SDF has been linked to ....**
  - **Lower fertilization, implantation, and pregnancy rates**
  - **Higher rates of miscarriage**
  - **More cycles of treatment, longer time course to conception**





## *Readily available commercial SDF assays*

- **Direct SDF measurement**
  - TUNEL
  - COMET
- **Indirect measurement**
  - Halosperm
  - SCSA



# *SDF: How to Treat?*

- Short abstinence (<24 hrs)
- Dahan et al 2021
  - < 3h abstinence
  - 55% of high SDF normalized
  - Age < 40 and anti-oxidant usage associated with largest SDF improvements



# *SDF: How to Treat?*

- Short abstinence (<24 hrs)
- Lifestyle factors
- Antioxidant usage
  - MVI
  - CoQ10



## *Patient #3 - “Bigmouth Strikes Again”*

- 38 yo male presents with primary infertility, 34 yo partner. No GYN issues. TTC 8 months. Desires three children. His functional medicine physician recommended a sperm DNA fragmentation and it returned 28% (Normal < 25%).
  - Repeat the frag?
    - Short abstinence interval
    - Antioxidant therapy
  - Use sperm sort device?
  - Skip IUI?
  - IVF with ejaculated?
  - TESE?





## *Variability of Sperm DNA Fragmentation*

- **Gonzalez-Martinez 2023 –**
  - SDF did not vary between 2,3, or 4 ejaculates
  - Higher (>30%) DNA fragmentation had more variability
  - Lower (<30%) had less variation
  - Mid-range (20-30%) less predictive of subsequent SDF
- **Kim et al 2022 –**
  - Three consecutive ejaculates on three consecutive days
  - Cancer pts cryopreserving
  - No significant SDF variations



## *Patient #4 - “It’s the End of the World as We Know It...”*

- 43 yo female who froze 12 eggs at age 36. Current AMH 0.5. Partner is 41, one child (12 yo) from prior relationship. TMS 5M, 42% fragmentation. Large left varicocele.
- SSD – four nonfragmented sperm after processing
- She has great IVF coverage but will be changing jobs in 3 months.



## *Live poll -*

- **Sperm source for the cryopreserved eggs?**
  - Ejaculated
  - TESE
  - Multiple ejaculates + SSD
- **Next step?**
  - Delay and let someone else worry about it?
  - Fix varicocele? Simultaneous TESE for vit eggs?
  - Try another fresh IVF for more eggs?
  - Thaw half the eggs and try IVF?



## *SDF and varicocele*

- **Many studies correlate varicocele and elevated SDF**
- **Mechanisms include scrotal hyperthermia, reflux of adrenal metabolites, and cadmium accumulation as ROS-generating stimuli**
- **ROS leads to lipid peroxidation and DNA damage**
- **Roque and Esteves 2018**
  - **Multiple studies, including three RCTs, show significant improvement in SDF pursuant to varicocele repair**
  - **Several studies show that the SDF improvement is greatest among couples achieving pregnancy**





# SDF and Varicocele Treatment

**Table 4. Characteristics of the meta-analyses assessing the effects of varicocelectomy on sperm DNA fragmentation**

Author, year, (country)	Population	Type of Included Studies	SDF assay	Varicocelectomy technique	Number of studies and participants	Decrease %SDF after varicocelectomy	Limitations
Wang et al, 2012 (China) (103)	Infertile men with palpable varicocele and abnormal SA	Retrospective and prospective cohort	SCSA, TUNEL and Comet	Open non-microsurgical and open microsurgical	6 studies; 177 participants	WMD -3.37%; 95% CI: -4.09 to -2.65, P<0.05	One study included men using antioxidants, and another study included adolescents; Data were pooled irrespective of SDF assay type; Pregnancy and live birth rates not evaluated
Qiu et al, 2020 (China) (144)	Men with varicocele	Prospective cohort and case-control	SCSA, SCD, TUNEL, Comet, and AOT	Open non-microsurgical and open microsurgical	11 studies; 394 participants	WMD -5.79%; 95% CI -7.39 to -4.19, P<0.05	One study included fertile men, another included men with subclinical varicocele; one study included adolescents, and another trial assessed SDF by a sperm chromatin protamination test; data was pooled irrespective of SDF assay type; pregnancy and live birth rates not evaluated
Birowo et al, 2020 (Indonesia) (147)	Infertile men with palpable varicocele	Prospective cohort	SCSA and TUNEL	Open non-microsurgical and open microsurgical	7 studies; 289 participants	WMD -6.86%; 95% CI -10.04 to -3.69, P<0.05	Low number of studies and participants; data was pooled irrespective of SDF assay type; pregnancy and live birth rates not evaluated
Lira Neto et al, 2020 (Brazil) (23)	Infertile men with palpable varicocele	Retrospective and prospective cohort	SCSA, SCD, TUNEL and Comet	Open non-microsurgical, open microsurgical, and laparoscopic	19 studies; 1070 participants	WMD -7.23%; 95% CI -8.86; -5.69; P<0.05	Pregnancy and live birth rates not assessed

AOT: Acridine orange test; SDF: Sperm DNA Fragmentation; %SDF: sperm DNA fragmentation rate; TUNEL: terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling; SCSA: sperm chromatin structure assay; SCD: sperm chromatin dispersion test; WMD: Weight Mean Difference



## *Patient #5 – “Don’t Look Back in Anger”*

- **48 yo male, father of three, had a vasectomy in 2014 and reversal two years ago. SA parameters normal. He and his partner (33) have conceived three times. All miscarried by week 12. RPL workup unrevealing. POC for 2/3 were euploid. Karyotypes for both normal. DNA fragmentation is 63%. Repeated on one day of abstinence + antioxidants – 54%. Post SSD – 34%.**



## *Live Poll – Snip-snap*

- Ejaculated sperm?
- TESE?
- Continue intercourse?
- IUI?



## *SDF and RPL*

- **Exact link has not been elucidated –**
- **Gosalves et al 2019**
  - **Excessive OS triggers base pairing abnormalities**
  - **Chromatin-protein cross linking**
  - **Oocyte repair mechanisms attempt to repair this prior to further development**
- **Ribas-Maynou 2019**
  - **Double stranded breaks more severe, associated w RPL**



## *Use of Testicular Sperm*

- **Lower fragmentation, better yield of blastocysts**
- **Theoretical risk of higher aneuploidy**
  - **Hervas et al 2022 – no change in embryo aneuploidy rate, and TESE sperm trended lower than EJ sperm**
  - **Moskovetsev et al 2012 – ejaculated vs TESE from 8 men with high SDF**
    - **Fragmentation rate lower in TESE (15% vs 48%)**
    - **Aneuploidy rate of TESE sperm higher (12.4% vs 5.7%)**
  - **Multiple studies imply that sperm from infertile/NOA men are at baseline more aneuploid**



## *Patient #6 – “True Faith”*

- 42 yo male. Normal SA parameters. 40 yo female partner, AMH 0.3.
- IUI x2 failed with reasonable post-wash yield.
- IVF – 2 eggs retrieved, 2 ICSI, no fert
- DNA fragmentation 38%, repeat w SSD – 18%
- Donor oocyte is not an option





## *Live Poll – 2 Peas in a Pod*

- **Repeat IVF with ejaculated**
- **Repeat IVF with TESE**
- **Continue IUI**
- **Recommend adoption**



## *Oocyte repair mechanisms*

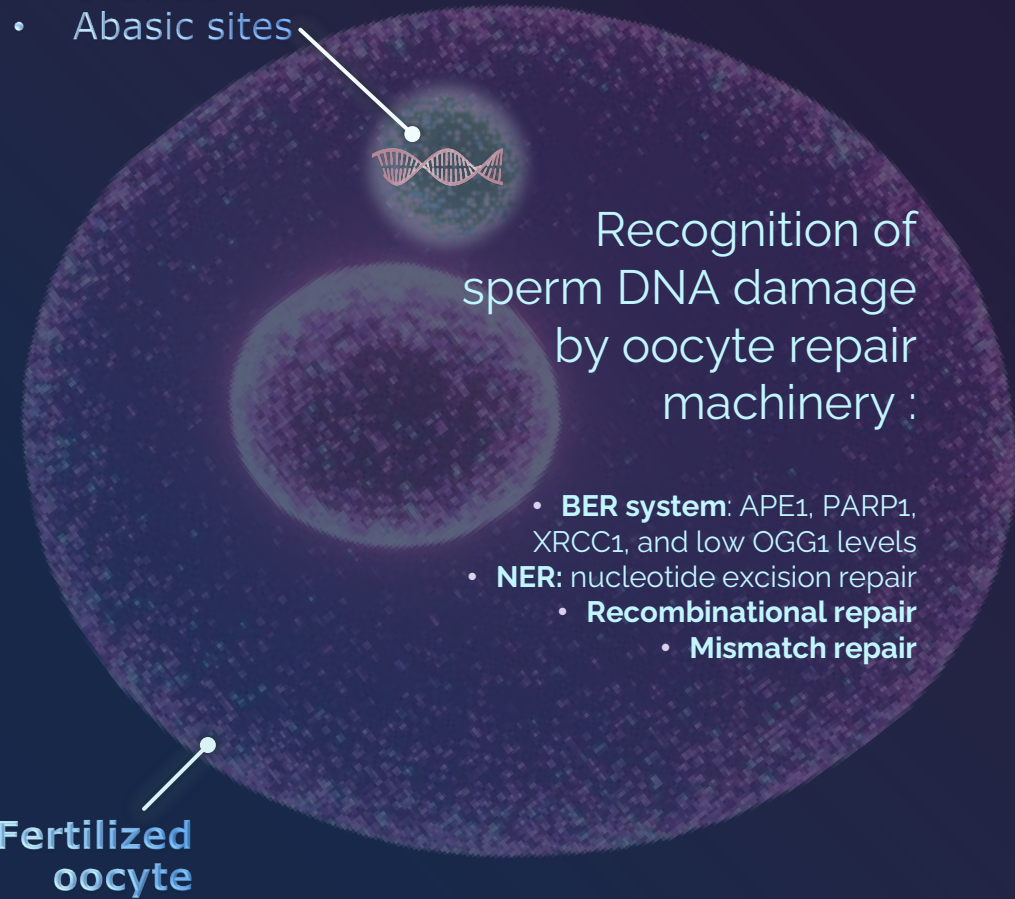
- Sperm with fragmented DNA retain their ability to fertilize (Zenzes 1999)
- Oocyte DNA repair mechanisms, if robust enough, can repair fragmented sperm and continue the process of normal embryo development
- Donor oocyte studies:
  - Esbert 2013
  - Anotnouli 2019
  - Hervas 2022
  - No differences in IVF outcomes for higher fragmented sperm



# Role of oocyte machinery to repair sperm DNA damage after fertilization

## DNA damage markers:

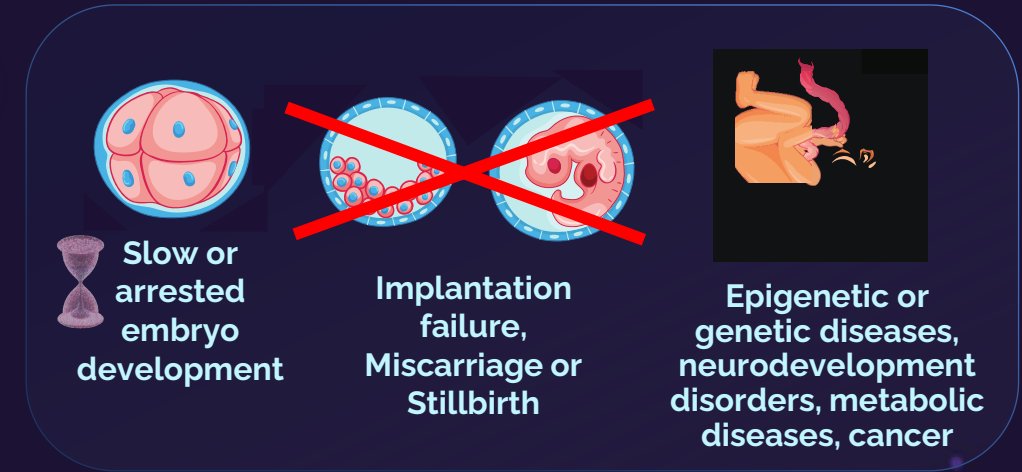
- 8-OHdG
- Abasic sites



Efficient repair  
and/or  
Low DNA  
damage/SDF



Oocyte repair  
failure  
and/or  
Excessive DNA  
damage/SDF



8-OHdG, 8-hydroxydeoxyguanosine; BER, Base excision repair; APE1, DNA (apurinic/apyrimidinic site) endonuclease 1; PARP1, poly (ADP-ribose) polymerase 1; XRCC1, x-ray cross-complementing protein

Adapted from Champroux A. et al. *Basic Clin. Androl.* 26, 17 (2016) (CC BY 4.0 License); Embryo and fetal graphics courtesy of Vecteesy.com and Freepik.com

## *SDF and AMA*

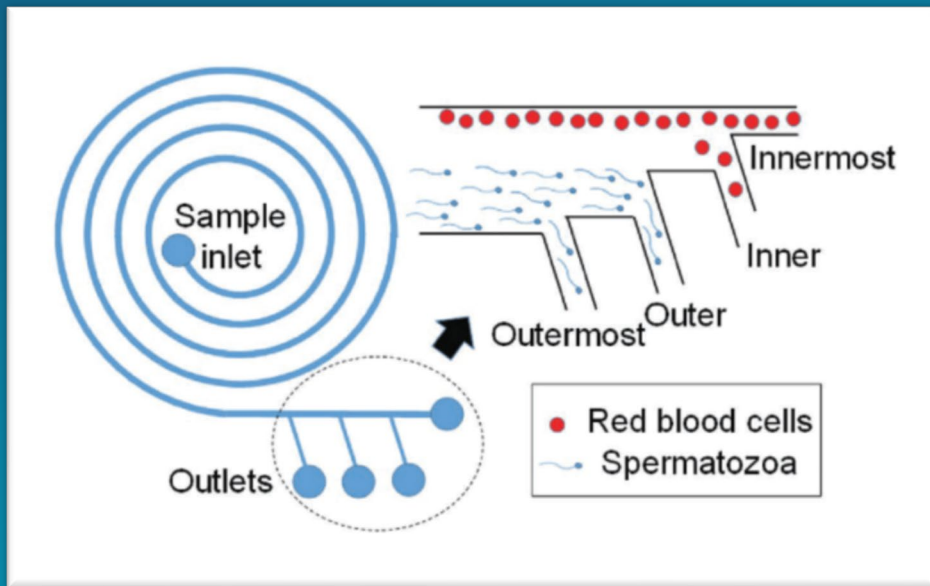
- **Khalafallah 2021**
  - 379 couples ICSI
  - Men – low (<20%), moderate (20-30%), and high
  - Women – Favorable (<35yo, AMH >7), and unfavorable
  - No difference in IVF outcomes for SDF <30%
  - Significantly lower CP and LB rates for high SDF and unfavorable age/AMH
- **Setti 2021**
  - 540 ICSI cycles
  - Pts grouped by maternal age and SDF
  - Female age >40 + SDF >30 % - fewer blasts, lower preg/imp rates
  - Female age <40, no effect of high SDF



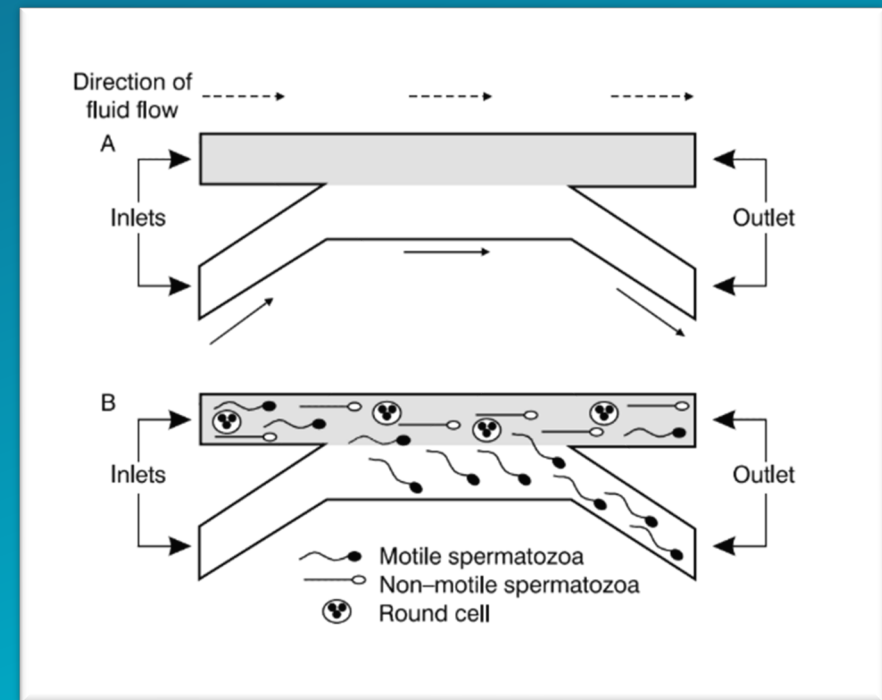


# Sperm sorting devices

- **Passive selection**
  - Size based, pushed through with fluid



- **Active selection**
  - Motility-based, rheotaxis



## *Sperm sorting devices*

- **Theory –**
  - **Compared to density gradient and centrifugation, the use of sperm sorting devices traumatizes the sperm less and therefore induces less DNA damage, leading to better results down the line as the cycle progresses**
  - **Zymot and Lenshooke**





# Comparison of SSDs - SA parameters

**Table 1** Assessment of semen quality after DGC, Zymot, and CAO for processing of normozoospermic specimens

Parameters		Normozoospermic (n=34)			
		Neat	DGC	Zymot	CAO
Concentration	Median (IQR) (M/mL)	38.5 (27.0-56.7)	6.5 (3.1-14.1) <sup>*a</sup>	4.8 (2.4-8.5) <sup>*b</sup>	5.7 (2.5-8.3) <sup>*c</sup>
	Change to neat (%)	-	-85.0 <sup>a</sup>	-89.2 <sup>b</sup>	-87.6 <sup>b</sup>
Total motility	Median (IQR) (%)	56.2 (51.6-68.7)	85.8 (78.7-91.2) <sup>*a</sup>	90.7 (76.9-95.5) <sup>*b</sup>	94.0 (91.3-95.9) <sup>*c</sup>
	Change to neat (%)	-	+40.0 <sup>a</sup>	+46.4 <sup>b</sup>	+57.6 <sup>c</sup>
Motile sperm count	Median (IQR) (M)	24.2 (14.6-34.8)	5.4 (2.4-13.3) <sup>*a</sup>	2.2 (0.9-3.6) <sup>*b</sup>	2.8 (1.2-3.9) <sup>*b</sup>
	Change to neat (%)	-	-79.9 <sup>a</sup>	-92.8 <sup>b</sup>	-90.2 <sup>b</sup>
Progressive motility	Median (IQR) (%)	47.4 (39.5-55.9)	80.6 (69.2-86.4) <sup>*a</sup>	85.6 (73.9-92.7) <sup>*b</sup>	90.8 (86.7-93.9) <sup>*c</sup>
	Change to neat (%)	-	+50.5 <sup>a</sup>	+64.8 <sup>b</sup>	+85.3 <sup>c</sup>
Rapid progressive motility	Median (IQR) (%)	35.7 (25.8-46.7)	75.8 (65.8-82.3) <sup>*a</sup>	77.7 (64.5-85.1) <sup>*a</sup>	83.6 (77.9-87.5) <sup>*b</sup>
	Change to neat (%)	-	+87.6 <sup>a</sup>	+97.7 <sup>a</sup>	+125.3 <sup>b</sup>
Slow progressive motility	Median (IQR) (%)	10.9 (8.7-13.8)	4.4 (3.1-5.4) <sup>*a</sup>	7.1 (4.1-8.9) <sup>*b</sup>	7.1 (4.8-9.7) <sup>*b</sup>
	Change to neat (%)	-	-64.4 <sup>a</sup>	-49.9 <sup>b</sup>	-38.4 <sup>b</sup>
Normal morphology rate	Median (IQR) (%)	5.5 (4.5-8.0)	8.1 (5.6-10.9) <sup>*a</sup>	8.1 (7.0-12.0) <sup>*b</sup>	10.3 (7.6-14.5) <sup>*c</sup>
	Change to neat (%)	-	+22.5 <sup>a</sup>	+47.7 <sup>b</sup>	+57.7 <sup>c</sup>
DFI	Median (IQR) (%)	18.5 (10.5-22.8)	11.8 (6.9-19.8) <sup>*a</sup>	3.7 (2.3-6.1) <sup>*b</sup>	2.4 (1.6-3.4) <sup>*c</sup>
	Change to neat (%)	-	-22.0 <sup>a</sup>	-76.1 <sup>b</sup>	-86.2 <sup>c</sup>
AR	Median (IQR) (%)	13.2 (9.3-17.9)	13.4 (8.0-18.4) <sup>a</sup>	6.5 (4.0-9.0) <sup>*b</sup>	4.7 (2.5-6.8) <sup>*c</sup>
	Change to neat (%)	-	-7.0 <sup>a</sup>	-51.6 <sup>b</sup>	-62.0 <sup>c</sup>
VCL	Median (IQR) (µm/s)	55.3 (42.6-58.5)	94.3 (79.1-108.0) <sup>*a</sup>	86.3 (80.0-92.2) <sup>*b</sup>	80.2 (75.3-98.5) <sup>*b</sup>
	Change to neat (%)	-	+78.1 <sup>a</sup>	+59.6 <sup>b</sup>	+67.9 <sup>b</sup>
ALH	Median (IQR) (µm)	4.5 (3.8-5.0)	6.2 (5.1-7.1) <sup>*a</sup>	6.2 (5.5-6.6) <sup>*a</sup>	5.5 (5.1-6.9) <sup>*a</sup>
	Change to neat (%)	-	+41.2 <sup>a</sup>	+40.7 <sup>a</sup>	+37.6 <sup>a</sup>
LIN	Median (IQR) (%)	42.8 (41.1-47.3)	35.5 (30.4-41.2) <sup>*a</sup>	34.5 (31.5-37.9) <sup>*a</sup>	32.5 (29.3-38.7) <sup>*a</sup>
	Change to neat (%)	-	-23.2 <sup>a</sup>	-22.6 <sup>a</sup>	-26.5 <sup>a</sup>



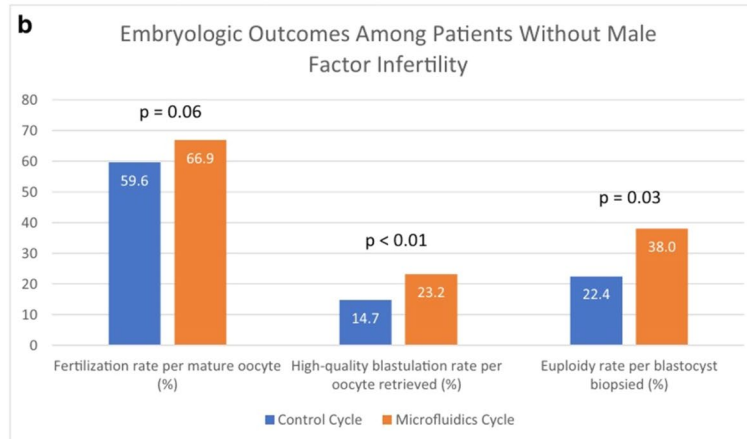
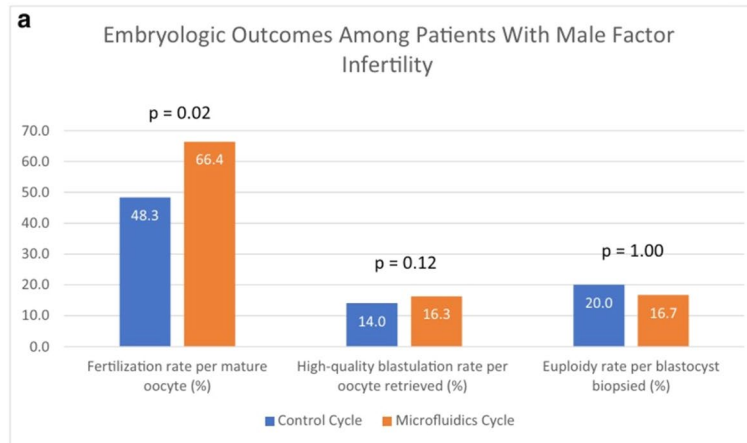
## *Clinical Implications of SSD*

- Quinn et al 2018 – significant reductions in SDF demonstrated
- Kalyan et al 2019 – no clinical difference in outcomes
- Quinn et al 2022 – randomized controlled trial, unselected population. No difference
  - Percentage of HQ blasts
  - Ongoing/clinical preg rate
- Godiwala et al 2022
  - Use of SSD improved fertilization, HQ blast yield per oocyte and per 2PN
  - For patients *with* male factor infertility – blast yield rate was not significantly different



# SSD outcomes

**Fig. 1 a)** Embryologic outcomes among patients with a diagnosis of male factor infertility. Twenty-seven subjects were included in the fertilization rate and blastulation rate analyses, while 5 subjects were included in the euploidy rate analysis. **b)** Embryologic outcomes among patients without a diagnosis of male factor infertility. Sixty-one subjects were included in the fertilization rate and blastulation rate analyses, while 15 subjects were included in the euploidy rate analysis



## *What's on the Horizon?*

- **PSFertility**
- **PATH Fertility – Sperm QT, epigenetics**
- **SNP Therapeutics**



## *PS Fertility*

- **Based in Charlottesville VA**
- **Phosphatidylserine is a necessary cog in the process of fertilization.**
- **PS score assesses PS presence in sperm, can be predictive of success after varicocele repair, even without traditional SA parameter changes**



# PS FERTILITY

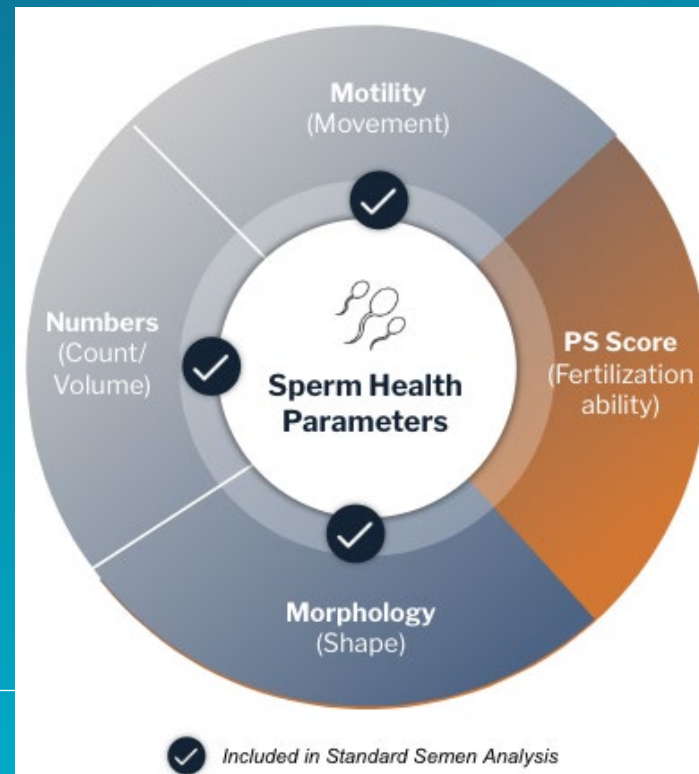
Building a clear future for male fertility

## PS Detect

*A novel test for sperm competency*

**PS Detect** is a flow cytometry based diagnostic test that detects the percentage of sperm capable of fertilizing an egg by identifying whether PS is present on each sperm - the **PS Score**.

Based on the findings published in *Nature Comm* (2019) by Rival et al., that phosphatidylserine (PS) on live sperm is essential for sperm-egg fusion.



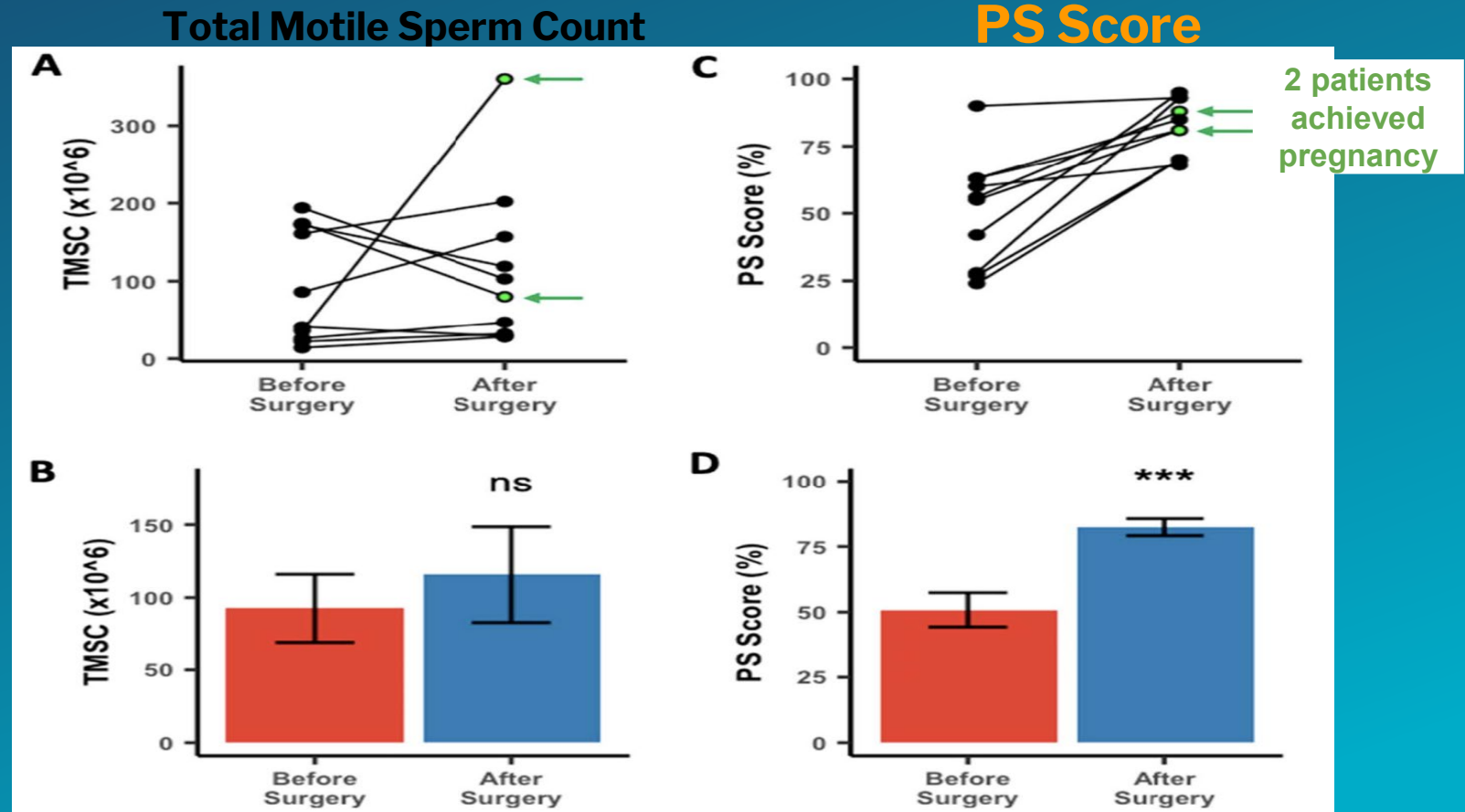
**PS Detect** along with the basic semen analysis provides a more complete picture of male fertility.



# PS Detect can guide decision making for varicocele repair

Opinion varies greatly within the urologist community on when and who should undergo a varicocele repair surgery.<sup>1</sup>

- Currently no diagnostic test to determine fertility and predict if a patient's fertility will improve from a varicocele repair
- Studies have shown pregnancy outcomes improve for spontaneous, IUI and IVF births following a varicocele repair<sup>2</sup>
- Varicocele repair is an underutilized treatment for male infertility



Varicocele repair (VR) resulted in an increase in **PS Scores** while TMSC varied. These results suggest that an increase in *PS positive live sperm* is the mechanism that improves male fertility following VR and PS Scores can be used to help guide decisions for VR.



# *Sperm Epigenetics*

- **SpermQT**

- **Measures the DNA methylation of 1,200 genes associated with sperm function.**
- **The higher the level of methylation, the worse quality**
- **Predictive of IUI/timed intercourse success or failure**
- **Sperm characterized as favorable, normal, or abnormal**
- **No differences with IVF outcomes across designations**



- **Genetic test that identifies a subset of men with decreased ATPase activity in their sperm**
- **Possible etiology for idiopathic infertility**
- **Increased sperm ATP activity through supplements**

