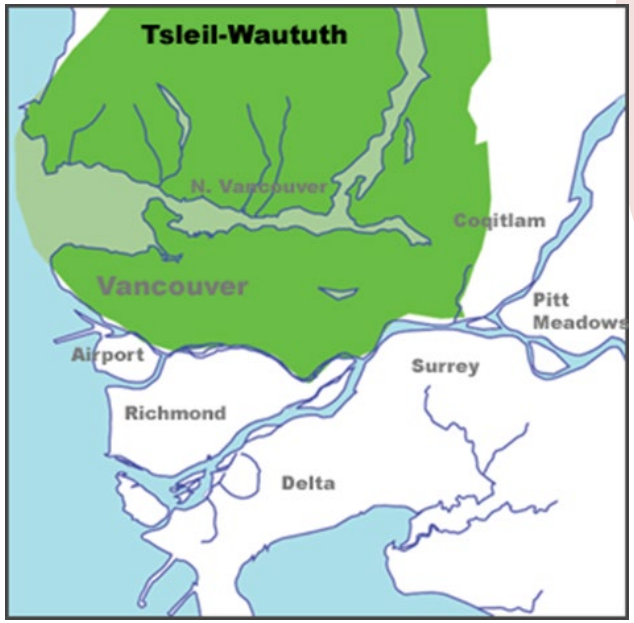
We would like to acknowledge that we are gathered today on the traditional territories of the Musqueam, Squamish and Tsleil-Waututh peoples.

Source: www.johomaps.net/na/canada/bc/vancouver/firstnations/firstnations.html



VCH Family Practice Rounds:

Updates in Fertility Care

JASON A HITKARI, MD, FRCS(C)
MEDICAL DIRECTOR, OLIVE FERTILITY CENTRE
DEPARTMENT OF OB/GYN, UBC

DISCLOSURES

- Co-own and operate a "private" fertility centre – will be showing some of the tools used in patient counselling.
- Recent past president and board member of the Canadian Fertility and Andrology Society
- Co-chair of the IVF Medical Directors Group

OJECTIVES

- To review the use of Anti-Mullerian Hormone (AMH) testing when assessing ovarian reserve
- To explain how ovarian reserve testing is used to understand current and future fertility and fertility planning
- To discuss fertility preservation (egg freezing and embryo freezing) with an emphasis on outcomes

Vignette

A 31-year-old patient with ovaries presents to your office hoping to have a "fertility check". They understand that age impacts fertility and they want an assessment.

What does this mean?

What is a “fertility check”?

- Difficult question to answer!

I would propose:

History can be helpful – PCOS? Pelvic surgery or infection? Dysmenorrhea?

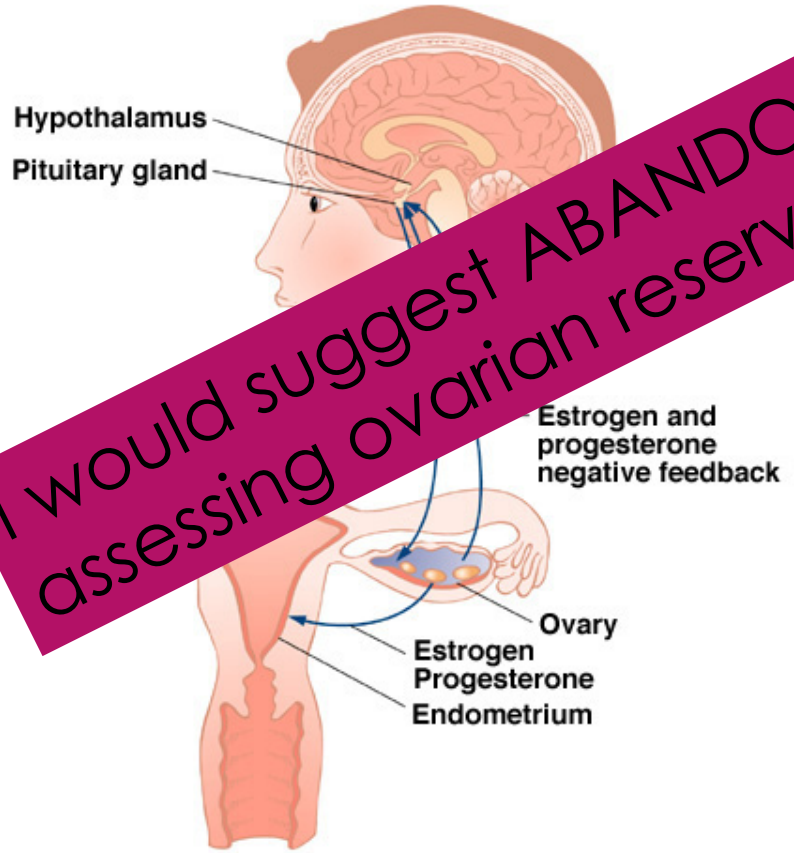
Exam/ultrasound – can detect fibroids and endometriomas

Ovarian reserve testing is key to this discussion.

Options for Ovarian Reserve Testing

- Age alone – *crude* assessment of ovarian reserve
- Day 3 FSH and estradiol levels
- Antral Follicle Counts (AFC) - requisition
- Anti-Mullerian Hormone (AMH) testing

What is wrong with day 3 FSH?



I would suggest ABANDONING this method of assessing ovarian reserve!

1. ates from month-to-month
2. Is dependent upon day of the month
3. Is dependent upon estradiol levels
4. Can be falsely *alarming*
5. Can be falsely *reassuring*

FERTILITY

Time is not on your side

A new hormone test helps women who didn't know they had to count their eggs if they want them to hatch

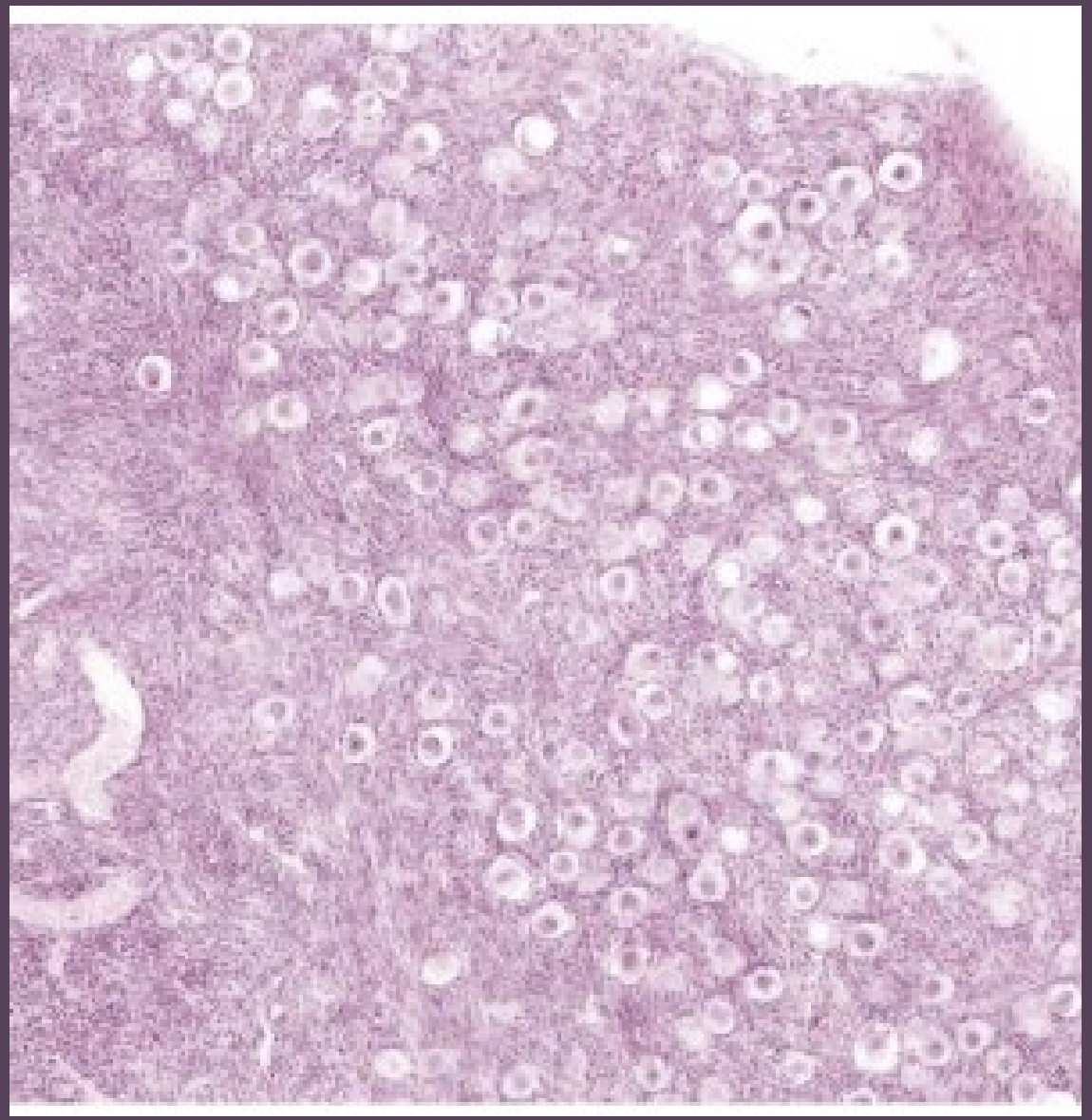
A WOMAN'S BIOLOGICAL clock is actually more like an hourglass that's turned over when she's born. Each grain of sand is one egg, and eventually they all run out. Rina Clarke had run through most of her eggs by last summer, when she was just 32. Sitting inside her fertility specialist's office, Clarke learned that a new test indicated she had a "low ovarian reserve" for her age. For a while, Clarke couldn't comprehend the doctor's message. But it was simple: fewer eggs equals fewer chances for babies. "I felt cheated—like, how is this possible? I'm a [young] woman, what do you mean I have this reserve issue?" she recalls. "You wind up in a position where you are disappointed and [asking], 'Why didn't anybody tell me this sooner?'"

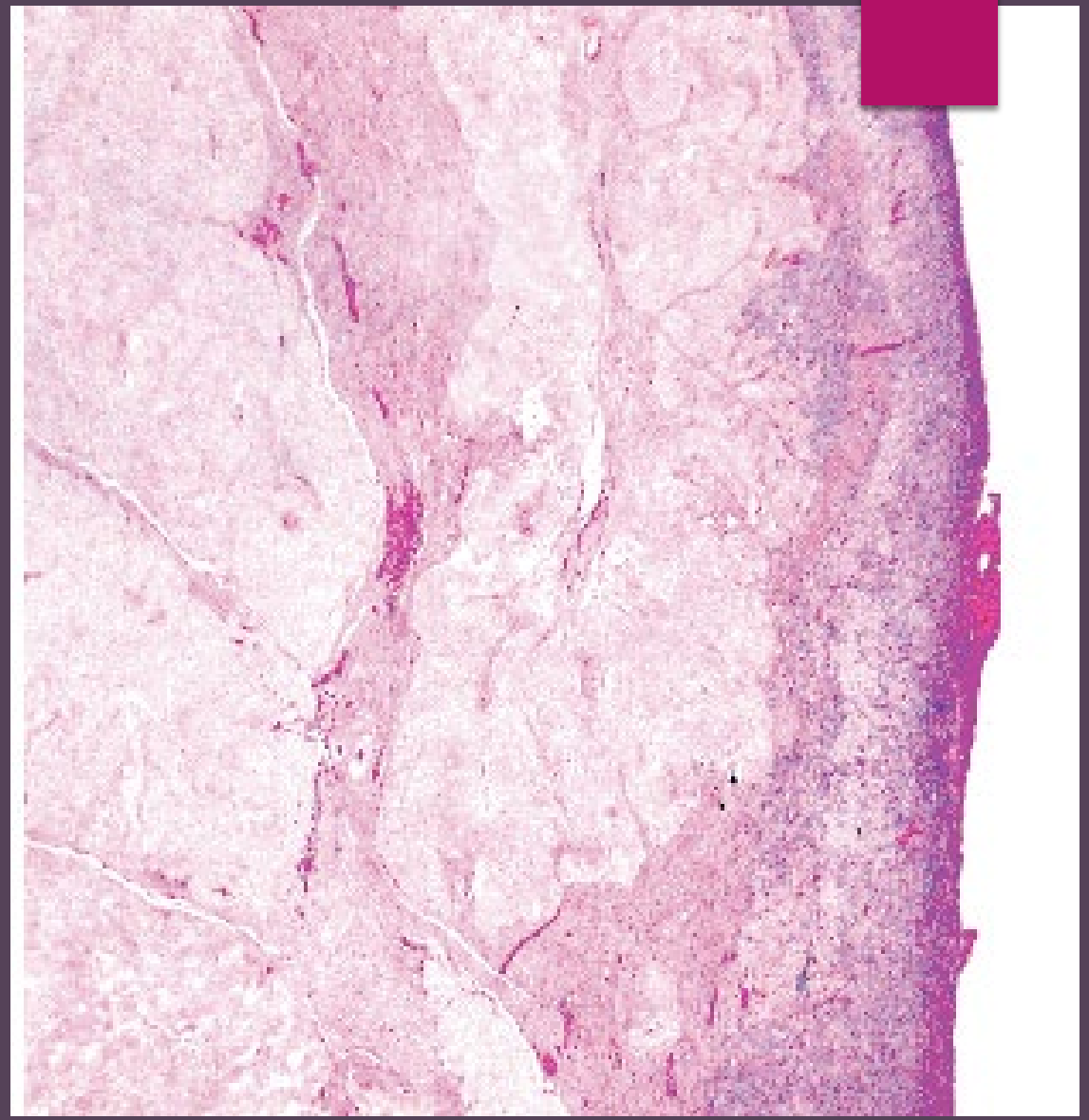
That test, which measures how much "anti-müllerian hormone" a woman produces in her ovarian follicles, is fast becoming the preeminent tool for fertility specialists in North America and Europe to determine the chances of their patients getting pregnant. "I [am] screamingly in favour of this test," says Dr. Tom Hannam of the Hannam Fertility Centre in Toronto, who has offered AMH testing for two years. "It's changed women's lives. It has absolutely changed my practice."

Until now, any woman who ever wondered about how many more years she could wait to have children—how many more dates she could go on before finding her ideal mate, how many more promotions she could attain, how many more professional letters she could add after her last name—had two choices: start trying and find out soon, or don't start trying yet and find out later. AMH testing promises to pinpoint her chances of getting pregnant today, how that might change, and whether there is anything to be done about it.

"It's a very good test because it tells people something about their biological clock that we really didn't have a widely available, accessible and reliable test for before" explains Dr. Beth Taylor, co-director of Genesis Fertility Centre in Vancouver and a professor at the University of British Columbia. "Information is very empowering. As a woman, I would want to know where I am on that fertility scale."

For $225 or less, a woman can find out by getting a blood test at any point during her menstrual cycle from a private clinic or lab. It reveals her level of AMH, which corresponds to the number of eggs she has left, or her "ovarian reserve." That declines with age, but not every woman is born with the same number of eggs or loses them at the

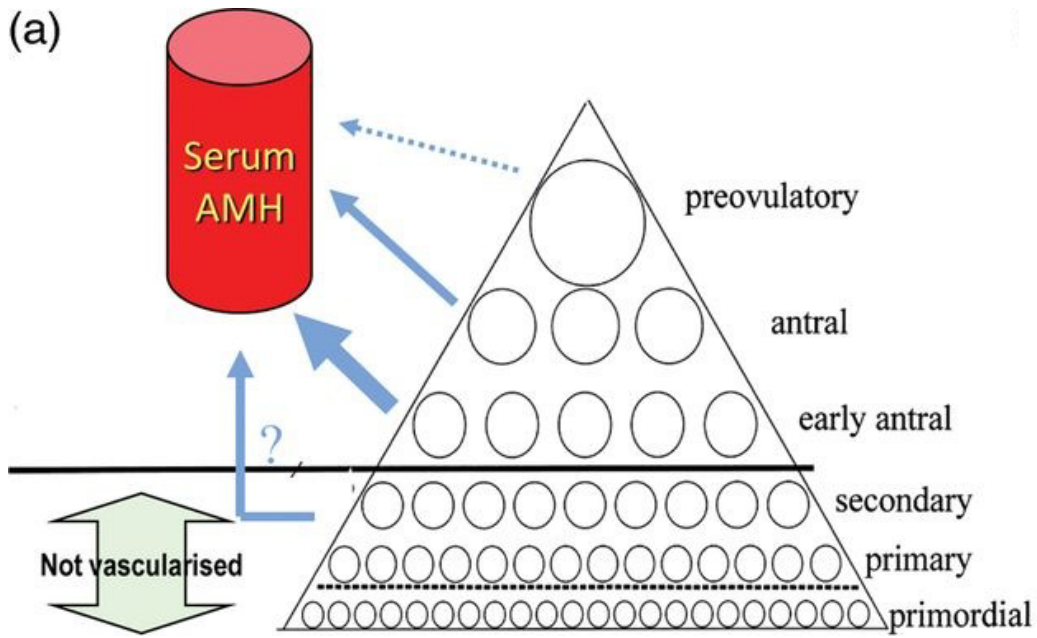




Follicular Development

- dimeric glycoprotein
- secreted by granulosa cells from primary to antral follicles[1]
- involved in ***slowing*** the process of follicle recruitment to the antral stage[2]
- ***disinhibition*** of dropping AMH allows for dominant follicle recruitment

1. Cate et al, Cell, 1986
2. Nilsson et al, Reproduction, 2007



Dewailly D et al. Hum. Reprod. Update 2014;20:370-385

Practicalities of ordering AMH

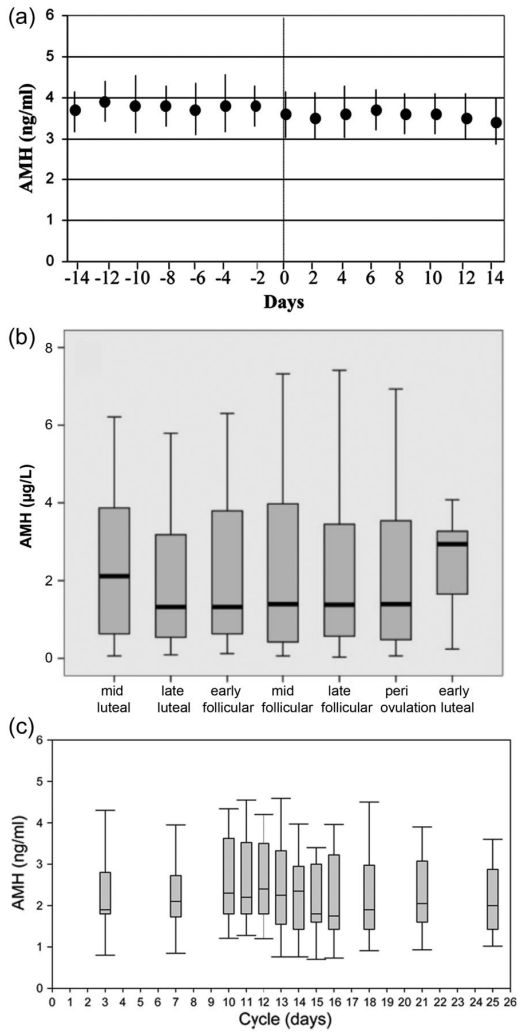
- NOT covered by MSP – current costs $78 at Lifelabs
- You need a graph to help interpret the result
- There are TWO assays and therefore TWO UNITS!

pmol/l ng/ml

- Lifelabs uses pmol/L

AMH variability throughout the menstrual cycle.

Intuitive since AMH is not made by the dominant follicle!



Dewailly D et al. Hum. Reprod. Update 2014;20:370-385

human reproduction update

Clinical use of AMH

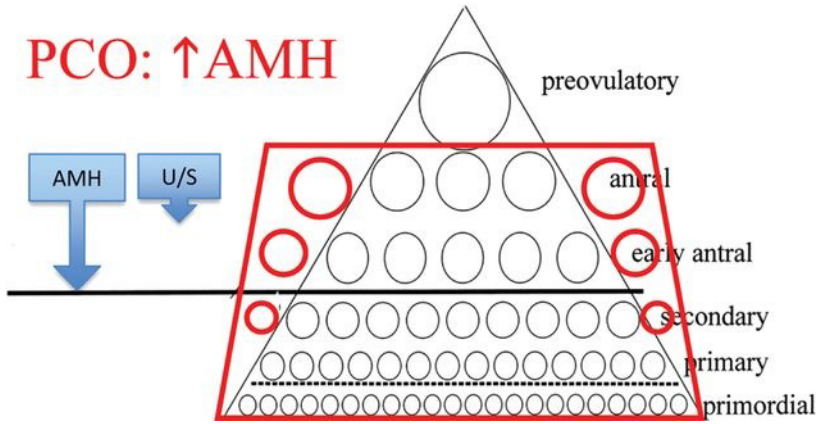
- Can be used to diagnose menopause
- Can be helpful in diagnosing PCOS
- OCP use causes a ***decline*** in AMH by 29.8 to 50% [2, 3]

1. van Dissledorp, et al, 2010
2. Bentzen et al, 2012
3. Kallio et al, 2013

AMH and PCOS

Oligo/Amenorrhea
Hirsutism/Acne
Ultrasound appearance of PCOS

- AMH levels 2-4x higher in PCOS women vs controls[1]
- production *per* granulosa cell is higher more follicles![2]

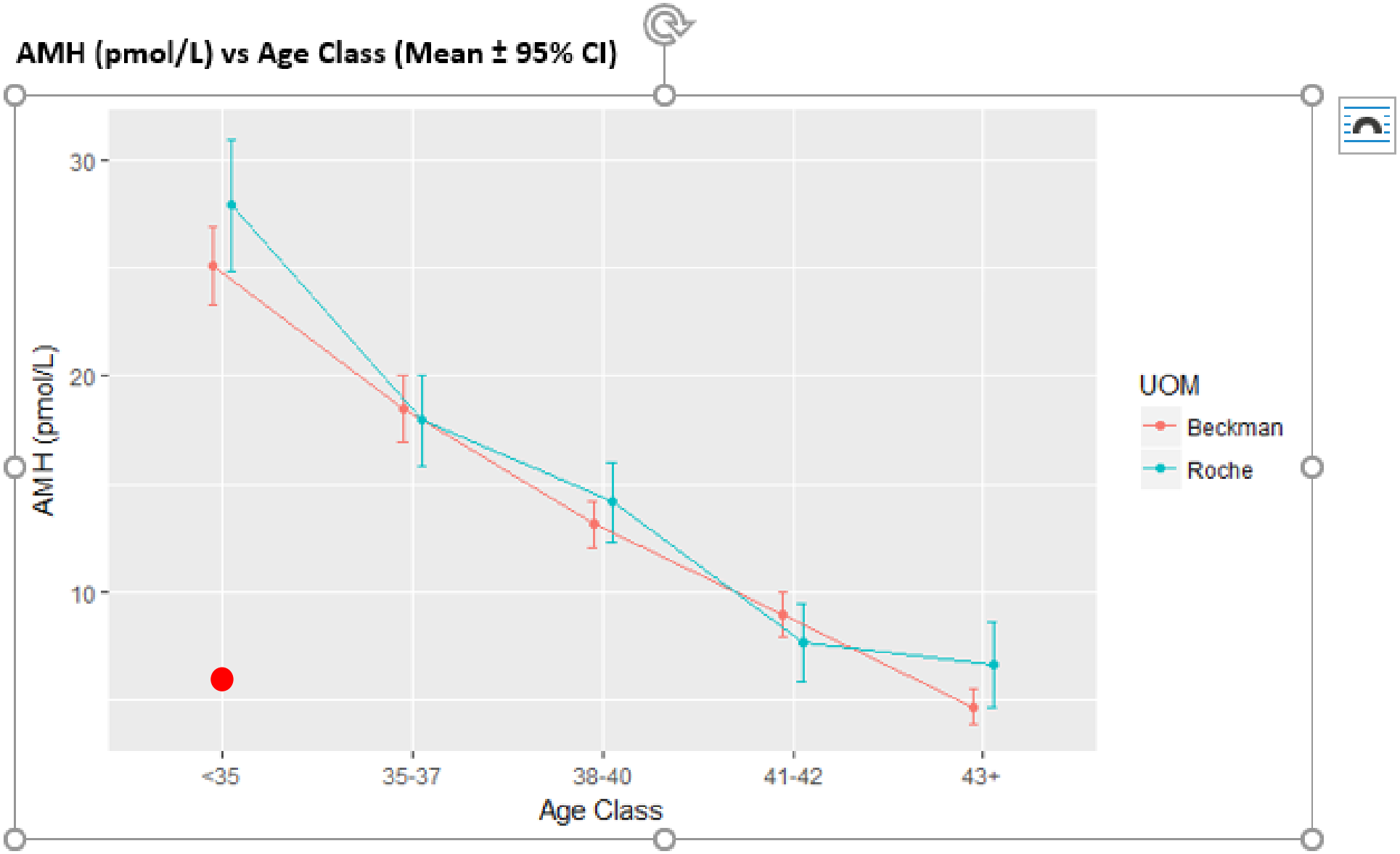


1. Park et al, 2010; Lie Fong et al, 2011
2. Pellatt et al, 2007

“Your 31-year-old patient’s history is unremarkable as is their exam/ultrasound. Their AMH level came back at 6.2 pmol/L.”

How do you *interpret* this result?

Observation	Result	Unit	Reference Range	Notes
Mullerian Inhibiting Substance	6.2	pmol/L	1.1-53.5 - N	AMH levels <5.0 pmol/L have a 63% probability of an antral follicle count (AFC) <8. AMH levels > 16.2 pmol/L have a 75% probability of an AFC >15 (Fertil Steril 2015 103:1074-1080). This AMH value in pmol/L was generated with the Elecsys AMH Plus assay and is suitable for the individualized dosing of follitropin delta. Status: Final


AMH (pmol/L) vs Age Class (Mean ± 95% CI)
AMH (pmol/L)
30
20
10
<35
35-37
38-40
41-42
43+
Age Class
UOM
Beckman
Roche

EGG NUMBER ≠ EGG QUALITY

This is a critical concept when counselling patients.

Egg quality can really only be determined in IVF

What is the point of measuring AMH then?

Time To Pregnancy in women 20-35 years of age..

AMH Levels	LOW (1st quantile)	MEDIUM (mid 2-4 quantile)	HIGH (5th quantile)
Number of patients	36	113	37
Median AMH pmol/L	10	22	55
Range of AMH pmol/L (conversion to ng/mL)	0-13	14-39	40-183

2012

Hagen *et al*, Fertility and Sterility, 2012

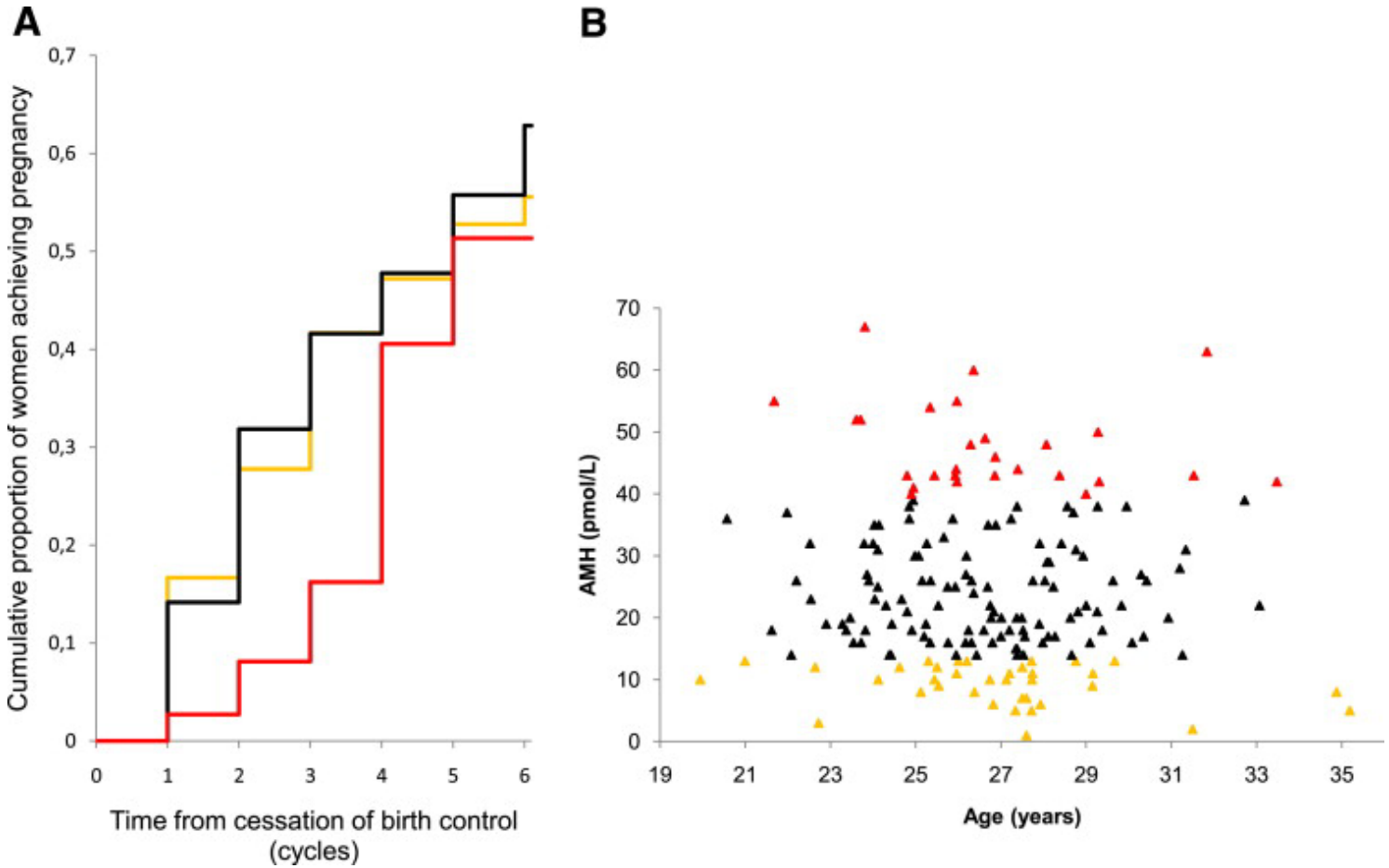


Figure 1 (A) Kaplan-Meier curves showing cumulative proportion of pregnancy by serum level of antimüllerian hormone (AMH). Low AMH (quintile 1) orange line , medium AMH (quintiles 2–4) black line , high AMH (quintile 5) red line . P value describes ...

The reason for measuring in this patient AMH is two-fold…

AGE	Monthly Pregnancy %
20	30 - 40
25	25-35
30	20-30
35	15-20
40	5-7%
45	1-2%

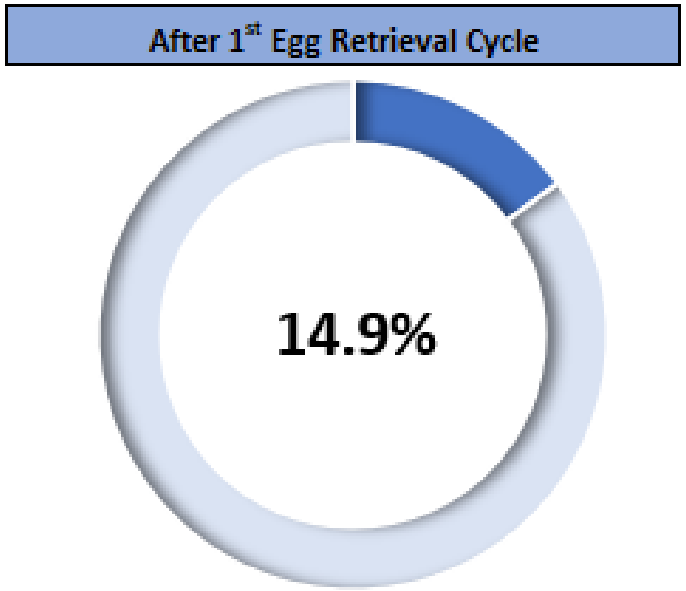
Dunson et al, Human Reproduction, 2002

The success of fertility treatments (superovulation or IVF) relies HEAVILY on a patient's ovarian reserve!

Imagine your 31-year-old patient is now 39 and trying to conceive with a partner with sperm but is having trouble.

Their AMH level is now 1.3 pmol/L.

SART Data (US) Livebirth Rate



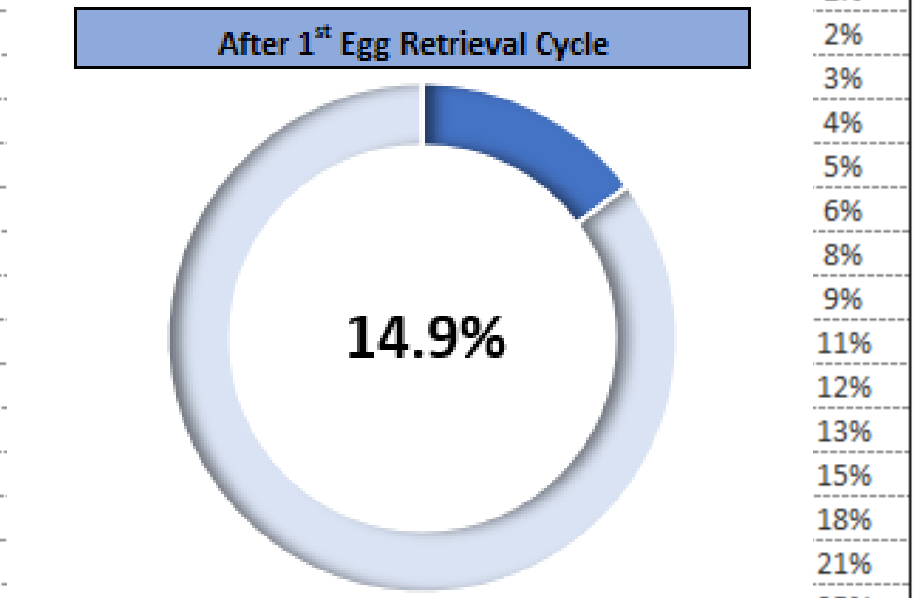
Patient:		35	Age @ Oocyte Retrieval	10	Mature Oocytes Retrieved

Probability of ≥ 1 live birth	69%	P (≥ 2 live births)	30%	P (≥ 3 live births)	9%

Probability (1 live birth)

Age @ Oocyte Retrieval — Dr. Jason Hitkari

Mature Oocytes Retrieved	########	≤35y	36y	37y	38y	39y	40y	41y	42y	43y	44y
1	13%	11%	9%	7%	6%	5%	4%	3%	2%	1%	1%
2	25%	21%	17%	13%	11%	9%	7%	6%	4%	3%	2%
3	34%	30%	24%	19%							2%
4	43%	37%	30%	24%							3%
5	51%	44%	36%	29%							4%
6	57%	50%	42%	34%							5%
8	68%	61%	52%	43%							6%
10	76%	69%	61%	50%							8%
12	82%	75%	66%	56%							9%
14	86%	81%	72%	62%							11%
16	89%	85%	77%	67%							12%
18	92%	88%	80%	71%							13%
20	94%	90%	84%	75%							15%
25	97%	95%	90%	82%							18%
30	99%	97%	93%	87%							21%
35	99%	98%	96%	91%	87%	82%	72%	64%	55%	40%	25%
40	>99%	99%	97%	94%	91%	86%	76%	69%	60%	44%	28%
45	>99%	99%	98%	96%	93%	89%	80%	73%	64%	48%	30%
50	>99%	>99%	99%	97%	95%	92%	83%	77%	68%	52%	33%
60	>99%	>99%	>99%	98%	97%	95%	88%	83%	74%	58%	38%
70	>99%	>99%	>99%	99%	98%	97%	92%	87%	80%	64%	43%
80	>99%	>99%	>99%	>99%	99%	98%	94%	90%	84%	69%	48%
90	>99%	>99%	>99%	>99%	>99%	99%	96%	93%	87%	73%	52%
100	>99%	>99%	>99%	>99%	>99%	99%	97%	95%	90%	77%	55%



“Your patient decides to undergo an egg freezing cycle….”

Same steps as an IVF cycle:

FSH injections for around 11 days, monitoring with ultrasound and blood work, and then a transvaginal egg retrieval under conscious sedation.

NON-INSURED SERVICES, PRICES IN CANADIAN AS OF JANUARY 2024 AND SUBJECT TO CHANGE

Medications:	$5,000- $9,000 per cycle (approximately) • Amounts will depend on how well medications are tolerated • All medications are non-refundable	Due at time of purchase
Cycle price:	$9,050/cycle • Cycle setup and coordination • Physician and nursing ongoing review • Blood work and ultrasound monitoring (for non-MSP patients some diagnostic blood tests and ultrasounds will be charged to you and are not covered under the IVF price) • Egg retrieval • Egg freezing • Egg assessment using Violet technology • Egg storage (one-year flat price)	Due at start of stim meds

Additional items (if applicable):

• Frozen egg storage after the first year (annual flat price)	$600	Due at anniversary date

Patient:		35	Age @ Oocyte Retrieval	10	Mature Oocytes Retrieved
Probability of ≥ 1 live birth	69%	P (≥ 2 live births)	30%	P (≥ 3 live births)	9%

Probability (1 live birth)

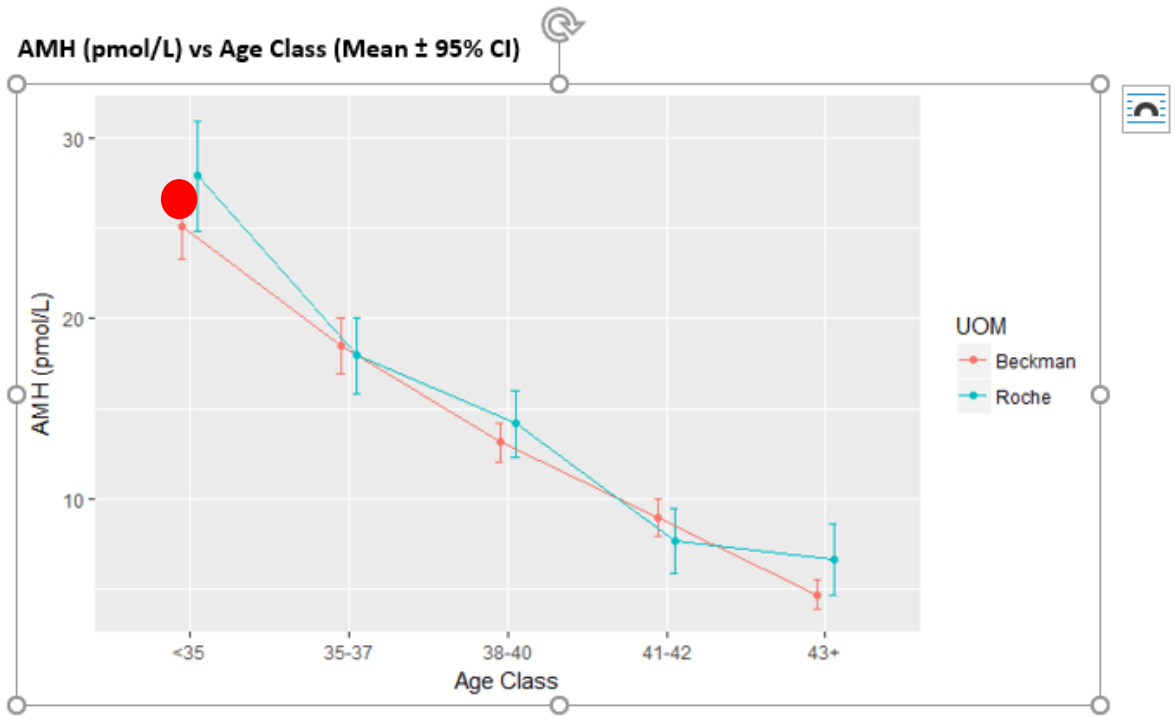
Dr. Jason Hitkari

Mature Oocytes Retrieved	Age @ Oocyte Retrieval										
	########	≤35y	36y	37y	38y	39y	40y	41y	42y	43y	44y
1	13%	11%	9%	7%	6%	5%	4%	3%	2%	1%	1%
2	25%	21%	17%	13%	11%	9%	7%	6%	4%	3%	2%
3	34%	30%	24%	19%	16%	14%	10%	8%	7%	4%	2%
4	43%	37%	30%	24%	21%	18%	13%	11%	9%	6%	3%
5	51%	44%	36%	29%	26%	22%	16%	14%	11%	7%	4%
6	57%	[illegible]	42%	34%	30%	26%	19%	16%	13%	8%	5%
8	68%	61%	[illegible]2%	43%	38%	33%	25%	21%	17%	11%	6%
10	76%	69%	6[illegible]%	50%	45%	39%	30%	25%	20%	14%	8%
12	82%	75%	6[illegible]%	56%	51%	45%	35%	30%	24%	16%	9%
14	86%	81%	72%	62%	56%	50%	40%	34%	27%	19%	11%
16	89%	85%	77%	67%	61%	55%	44%	37%	31%	21%	12%
18	92%	88%	80%	71%	65%	59%	48%	41%	34%	23%	13%
20	94%	90%	84%	75%	69%	63%	51%	44%	37%	25%	15%
25	97%	95%	90%	82%	77%	71%	59%	52%	43%	31%	18%
30	99%	97%	93%	87%	83%	77%	66%	58%	49%	36%	21%
35	99%	98%	96%	91%	87%	82%	72%	64%	55%	40%	25%
40	>99%	99%	97%	94%	91%	86%	76%	69%	60%	44%	28%
45	>99%	99%	98%	96%	93%	89%	80%	73%	64%	48%	30%
50	>99%	>99%	99%	97%	95%	92%	83%	77%	68%	52%	33%
60	>99%	>99%	>99%	98%	97%	95%	88%	83%	74%	58%	38%
70	>99%	>99%	>99%	99%	98%	97%	92%	87%	80%	64%	43%
80	>99%	>99%	>99%	>99%	99%	98%	94%	90%	84%	69%	48%
90	>99%	>99%	>99%	>99%	>99%	99%	96%	93%	87%	73%	52%
100	>99%	>99%	>99%	>99%	>99%	99%	97%	95%	90%	77%	55%

How do you counsel now?

Question	Thoughts
When would they use the oocytes?	If trying “at home” hasn’t work and the prognosis with IVF is low.
How long can oocytes be frozen?	Limit is unknown but easily >10 years
Do people use oocytes to help with their second child?	Yes

What if the case had been a 31-year-old person with ovaries with an AMH of 27.6 pmol/L?



IMPORTANT TO NOTE

LIVEBIRTH rates with egg freezing are not appreciably different if patient is 35 years old or younger.

“34-year-old patient with ovaries and their partner who makes sperm. Not wanting to conceive now but hoping to start in the next five years. Ideally, they want two children….”

If they are committed, better to cryopreserve EMBRYOS rather than eggs.

12 eggs generally creates 4 embryos **each** with a 45% chance of a livebirth.

12 eggs frozen would give them a chance of livebirth of 75%

Some data on how often patients are freezing eggs.

Nationally – CARTR Data

2013 → 203 patients froze eggs electively and for oncologic fertility preservation

2022 → 1735 elective egg freezing

405 egg/embryo for oncology

Year	Egg Freezing Cycles at Olive
2013	6
2014	16
2015	21
2016	59
2017	68
2018	113
2019	123
2020	160
2021	207
2022	230
2023	335

Oocyte Cryopreservation: A 9-Year Single-Centre Experience

R. Harjee

Rahana Harjee, MD;[1] Jing Chen, MSc;[2] Jeff Caudle, MSc;[2] Nadia Ouhibi, MSc, PhD;[2] Sara Edsall, MSc;[2] Justin Smrz, BSc;[2] Justin Lardizabal, MSc, PhD;[2] Salah Abdelghadir, MSc, PhD;[2] Gary Nakhuda, MD[1,2]

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[2]Olive Fertility Centre, Vancouver, BC

ABSTRACT

Objective: Oocyte cryopreservation (OC) has increased in recent years; however, there is a paucity of published data on the use cryopreserved oocytes and associated outcomes.

Methods: A retrospective review of 748 OC cycles between 2013 and 2022 at a private fertility centre was performed. Outcome parameters for oocyte retrieval cycles were reviewed. For patients who returned for oocyte disposition, outcomes subsequent to oocyte re-warming, fertilization, and transfer were analyzed.

RÉSUMÉ

Objectif : La cryoconservation d'ovocytes (CO) a gagné en popularité dans les dernières années; cependant, il y a très peu de données publiées sur l'utilisation des ovocytes cryoconservés et les résultats qui en découlent.

Méthodologie : Une étude rétrospective de 748 cycles de CO entre 2013 et 2022 a été menée dans une clinique de fertilité privée. Les critères de jugement pour les cycles de prélèvement d'ovocytes ont été examinés. Pour les patientes qui sont

J Obstet Gynaecol Can 2022;■(■):1–8
https://doi.org/10.1016/j.jogc.2022.10.006

Patient:		41	Age @ Oocyte Retrieval	6	Mature Oocytes Retrieved

Probability of ≥ 1 live birth	16%	P (≥ 2 live births)	1%	P (≥ 3 live births)	<1%

Probability (1 live birth)

Age @ Oocyte Retrieval

Dr. Jason Hitkari

Mature Oocytes Retrieved	Egg Donor	≤35y	36y	37y	38y	39y	40y	41y	42y	43y	44y
1	13%	11%	9%	7%	6%	5%	4%	3%	2%	1%	1%
2	25%	21%	17%	13%	11%	9%	7%	6%	4%	3%	2%
3	34%	30%	24%	19%	16%	14%	10%	8%	7%	4%	2%
4	43%	37%	30%	24%	21%	18%	13%	11%	9%	6%	3%
5	51%	44%	36%	29%	26%	22%	16%	14%	11%	7%	4%
6	57%	50%	42%	34%	30%	26%	19%	**16%**	13%	8%	5%
8	68%	61%	52%	43%	38%	33%	25%	21%	17%	11%	6%
10	76%	69%	60%	50%	45%	39%	30%	25%	20%	14%	8%
12	82%	75%	66%	56%	51%	45%	35%	30%	24%	16%	9%
14	86%	81%	72%	62%	56%	50%	40%	34%	27%	19%	11%
16	89%	85%	77%	67%	61%	55%	44%	37%	31%	21%	12%
18	92%	88%	80%	71%	65%	59%	48%	41%	34%	23%	13%
20	94%	90%	84%	75%	69%	63%	51%	44%	37%	25%	15%
25	97%	95%	90%	82%	77%	71%	59%	52%	43%	31%	18%
30	99%	97%	93%	87%	83%	77%	66%	58%	49%	36%	21%
35	99%	98%	96%	91%	87%	82%	72%	64%	55%	40%	25%
40	>99%	99%	97%	94%	91%	86%	76%	69%	60%	44%	28%
45	>99%	99%	98%	96%	93%	89%	80%	73%	64%	48%	30%
50	>99%	>99%	99%	97%	95%	92%	83%	77%	68%	52%	33%
60	>99%	>99%	>99%	98%	97%	95%	88%	83%	74%	58%	38%
70	>99%	>99%	>99%	99%	98%	97%	92%	87%	80%	64%	43%
80	>99%	>99%	>99%	>99%	99%	98%	94%	90%	84%	69%	48%
90	>99%	>99%	>99%	>99%	>99%	99%	96%	93%	87%	73%	52%
100	>99%	>99%	>99%	>99%	>99%	99%	97%	95%	90%	77%	55%

Summary Points

- Clearly, the number of patients seeking "fertility assessments" is on the rise
- Ovarian reserve testing is a key part of this assessment
  - AMH is the preferred method of assessing ovarian reserve
- If a patient with ovaries is under 35 with a normal AMH level, it is reasonable to counsel them to wait to freeze eggs (reassure)
- If a patient with ovaries has a low AMH, they should consider freezing their eggs because the more eggs frozen, the better the chance for livebirth

Summary Points

- Use this knowledge about AMH to help counsel people trying at home or considering donor insemination
- Embryo freezing has a higher cumulative livebirth rate than oocyte freezing
  - Patient can use anonymous donor sperm, known donor sperm, or partner's sperm
- AMH levels are useful in other clinical scenarios such as confirming menopause or helping to diagnose PCOS

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