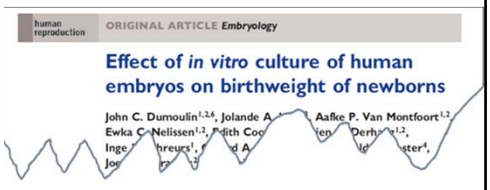
Embryo Culture Revisited

Jason E. Swain, PhD, HCLD
Fertility Lab Sciences

Improving Culture Media



Culture Media

- Several media utilized in an IVF lab
- Each must consider the specific requirements of the respective cells
  - sperm
  - cumulus-oocyte-complex
  - denuded oocyte
  - cleavage embryo
  - post-compaction embryo
- Many companies, each with multiple media & related products for the same procedural steps
  - Oil *(mineral, paraffin, light, washed)*
  - Protein *(HSA, recHSA, globulins)*
- Other culture environment variables

Sperm Isolation
Sperm Washing
Oocyte Collection
Oocyte Maturation
Oocyte Denuding
Insemination / ICSI
Embryo Culture
Biopsy
Transfer
Cryopreservation
Thawing

Human Reproduction Update, Vol.19, No.3 pp. 210–220, 2013
Advanced Access publication on February 5, 2013 doi:10.1093/humupd/dms061

human reproduction update

Embryo culture media and IVF/ICSI success rates: a systematic review

E. Mantikou[1], M.A.F.M. Youssef[1,2,3], M. van Wely[1], F. van der Veen
H.G. Al-Inany[2], S. Re[illegible][1], and S. Mastenbroek[1,*]

RESULTS: Twenty-two RCTs were included that evaluated 31 different comparisons. Conventional meta-analysis was not possible for any of the outcomes as nearly all trials compared different culture media. Only four trials reported on live birth, and one of them reported a significant difference. Nine trials reported on ongoing and/or clinical pregnancy rates, of which four showed a significant difference. Pooling the data did not reveal a superior culture medium.

"…did not reveal a superior culture medium"

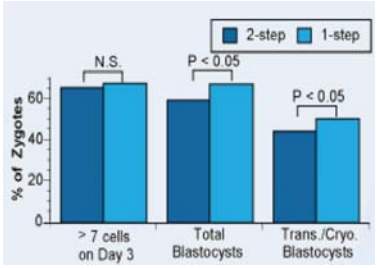
Media as a Therapeutic Agent

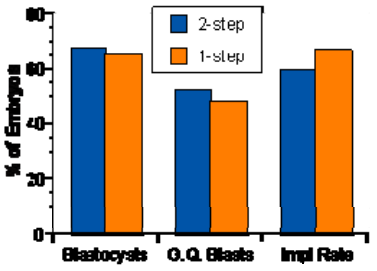
- Specific medium for specific patients/populations
  - -Database of commercial media performance for specific patients/diagnoses?
  - -Therapeutic additives for specific patients
    - *some commercial media already include GM-CSF or insulin*
- Embryo-specific media (the embryo as the patient)
  - -molecular profiling of spent media
  - -identify & add embryo-trophic secreted factors
  - -customize substrate profile for specific embryos
  - -other additives *(macromolecules, vitamins, etc)*

One medium may not be optimal for all embryos

Uninterrupted Culture

- Medium renewal every 48-72h
  - Prevent substrate depletion,
  - Remove ammonium
  - Remove other byproducts
  - Reduce concern of VOC accumulation
- Uninterrupted Culture 5-6 days
  - Accumulation of "good" factors
  - Less stress from handling
  - Useful for time-lapse imaging
  - *Requires dipeptide glutamine*
  - *Requires low oxygen/VOC free gas/air*





Several single-step media now available

Embryo Culture Media

- Each approach has its criticisms & limitations
- Embryos develop well in various media
- Distinguish “fact” from “fetish”

Developmental plasticity ***(but can be exceeded)***

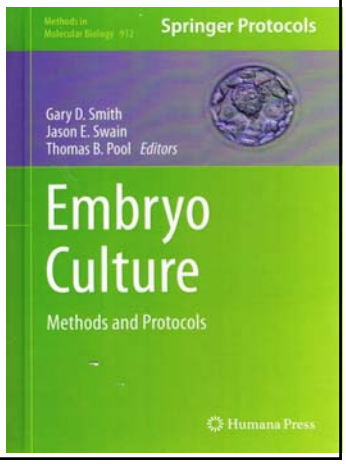
Determine “best” product in your own lab

The Culture System

- Other factors can influence embryo development and culture media efficacy – must be considered when evaluating
  - Contact materials/toxicity
  - Group embryo culture vs. individual
  - Incubator type/management
  - Low O2 vs. atmospheric O2
  - Air quality/VOCs
  - Technician

The medium is just one component!

(generally well-controlled)

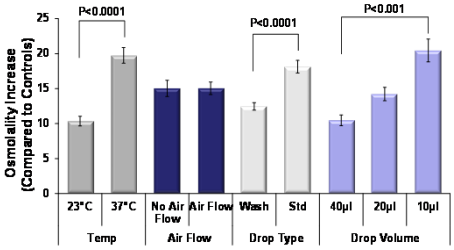


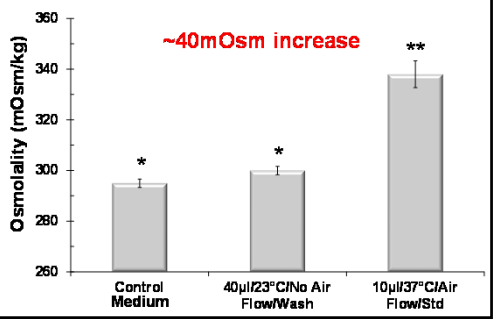
Lab Controlled Media Variables

IVF laboratories can impact efficacy of culture media

Osmolality

- Proper media osmolality ~260-290mOsm
- >300mOsm can inhibit embryo development *in vitro* (Hadi et al. 2005)
- Lab technique can inadvertently raise media osmolality (Swain et al. 2012)





pH

- pHo higher than pHi to combat acidification (~7.2)
  - Human embryo pHi is ~7.1 -7.2 (Phillips et al. 2000)
- <7.4 to avoid reduced development
- No proven need to change pHo during embryo culture (Swain 2012)
  - Slightly higher pHo/bicarbonate may benefit sperm/fertilization
  - Later stage embryos may do better with higher bicarb (pHo)
  - Later stages regulate acidic pHi more effectively
  - Uterus appears more acidic that oviduct
- Optimum pHo likely varies from medium to medium
  - Ingredients can impact pHi independently from pHo (lactate, AAs)

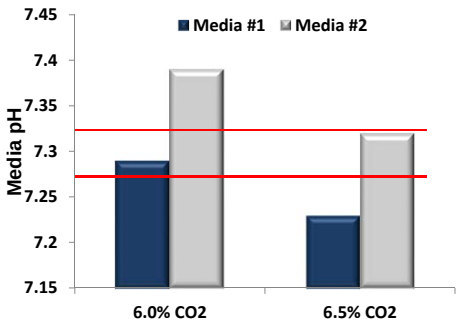
Must measure pH at some point (correctly)
Maintain a narrow and stable pHo

pHo Measurement

Same Basal Medium- Different Companies

Commercial Medium (HEPES-HTF)	pH @ 37°C (mean ± SEM)
Medium #1	7.28 ± 0.005
Medium #2	7.27 ± 0.003
Medium #3	7.26 ± 0.003
Medium #4	7.08 ± 0.007
Medium #5	7.08 ± 0.005

Same Medium – Same Company
w/ protein added or adding your own

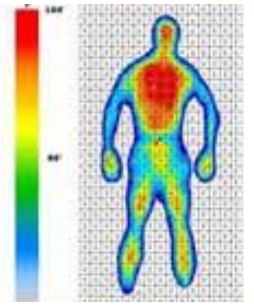


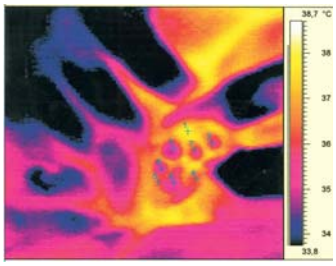
Swain et al. 2013

Temperature

- Question as to what is the best temperature to use in the IVF lab for gametes and embryos
- Body temperature 36.6-37.3ºC
  - Most use 37ºC
- Estimated temp inside the follicle is ~2.3°C cooler than core body temp
  Grinstead *et al., 1985*
- Animal data indicate a potential temp gradient in the fallopian tube 1.5° cooler than core body temp David et al. 1971, Hunter & Nichols 1986

Should we culture @ <37°C?





TECHNIQUES AND INSTRUMENTATION

FERTILITY AND STERILITY®
VOL. 77, NO. 6, JUNE 2002

Rigorous thermal control during intracytoplasmic sperm injection stabilizes the meiotic spindle and improves fertilization and pregnancy rates

Wei-Hua Wang, Ph.D.,[a] Li Meng, Ph.D.,[b] Richard J. Hackett, Rudolf Oldenbourg, Ph.D.,[d] and David L. Ke[illegible] M.D.

System 1: 34°C

System 2: 37°C

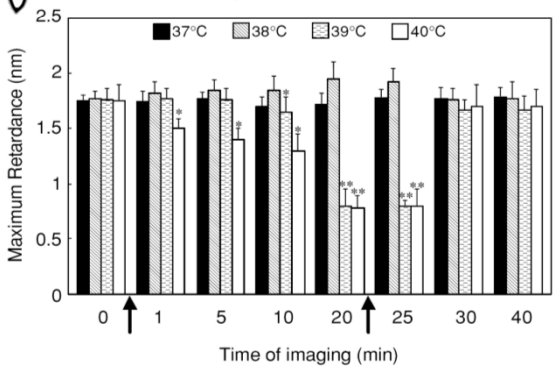
System 3: 33°C

	System 1	System 2	System 3
No. of patients	40	29	52
Average patient's age	33.8 ± 4.4	34.1 ± 4.6	34.1 ± 4.4
Average no. of cycles	2.3 ± 1.4	2.8 ± 1.2	2.6 ± 1.8
Day 3 FSH	6.1 ± 1.8	6.3 ± 2.6	6.2 ± 2.5
E_2 level (pre-hCG)	1346.4 ± 608.3	1344.8 ± 552.4	1417.6 ± 763.5
E_2 level (day for hCG)	1780.3 ± 805.1	1809.0 ± 815.6	1926.8 ± 980.8
No. of eggs examined	402	298	433
No. of eggs/patient	8.3	10.0	10.3
Eggs with spindle (%)	61.4[a]	81.2[a]	NA
Fertilization rate (%)	56.7[a]	78.8[a]	64.0[a]
Pregnant rate (%)	25.0[a]	51.7[a]	23.1[a]

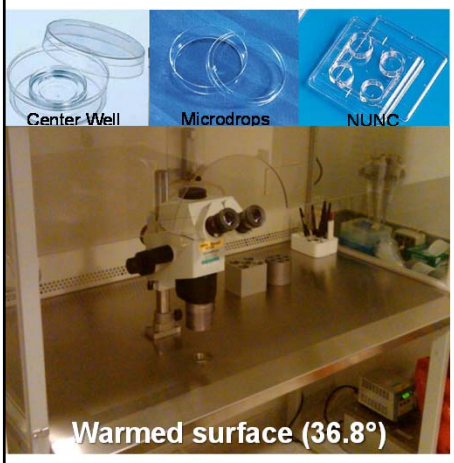
Zygote **12** (February), pp. 65–70. © 2004 Cambridge University Press
DOI:10.1017/S0967199404002631 Printed in the United Kingdom

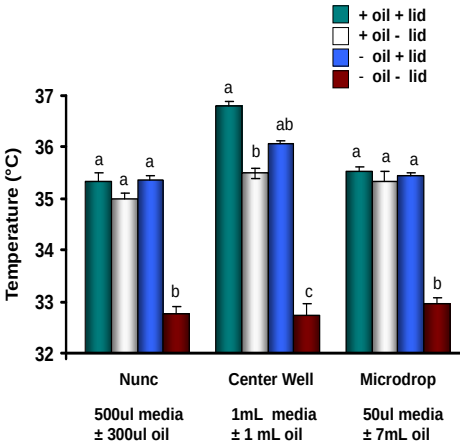
Overheating is detrimental to meiotic spindles within *in vitro* matured human oocytes

Xiao-Fang Sun[1], *Wei-Hua Wang*[2] *and David L. Keefe*[3]
Guang-Zhou Second Hospital, G[illegible]g-Dong, China; Tomball Regi[illegible]
[illegible]



Temperature





Examining the temperature of embryo culture in in vitro fertilization: a randomized controlled trial comparing traditional core temperature (37°C) to a more physiologic, cooler temperature (36°C)☆

Kathleen H. Hong, M.D.,[a,b] Hokyu
and Richard T. Scott Jr., M.D.,
* Departm
Brunswic

	MII's (n)	Fert Rate	Day 3 Cell #	Blast Rate	Usable Blast Rate	Aneuploidy Rate	Implantation
36°C	399	86.2%	7.0±0.1[a]	51.6%[a]	41.2%[a]	42.5%	67.4%
37°C	406	82.0%	7.7±0.1[b]	60.1%[b]	48.4%[b]	46.1%	73.3

Low O_2 & Embryo Culture

- Used extensively in various animal models
  - mouse, cat, sheep, pig, cow, rat
- Confounding variables sometimes "muddies" the waters of results in existing studies
  - Length of time, incubator, endpoint assessment, etc

Are there any publications where low O_2 *decreases* embryonic development or other measured parameters? NO!

Low O_2 & Human Embryos

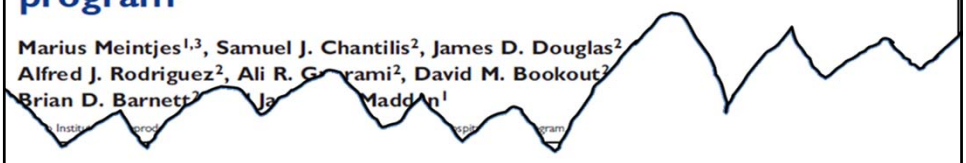
- Dumoulin et al. 1995 Fert Steril 63:115-119
- Dumoulin et al. 1999 Hum Reprod 14:464-469
- Dumoulin et al. 2000 Hum Reprod 15:402-409
- Catt and Henman 2000 Hum Reprod 15(suppl 2):199-206
- Bahceci et al. 2005 RBMonline 11:438-443
- Bedaiwy et al. 2004 Fertil Steril 82:593-600
- Bedaiwy et al. 2006 Fertil Steril 86:304-309
- Petersen et al. 2005 Acta Obstet Gynecol Scand 84:1181-1184
- Kea et al. 2007 Fertil Steril 87:213-216
- Anderson et al. 2007 Fertil Steril 88(suppl 1):S91
- Waldenstrom et al. 2009 Fertil Steril 91:2461-2465
- Kovacic and Vlaisavljevic 2008 RMBonline 17:229-236
- Meintjes et al. 2009 Hum Reprod 24:300-307
- Ciray et al. 2009 Fertil Steril 91(4 Suppl):1459-61
- Higdon et al. 2009 J Clinical Embryology (Fall) 12:6-11
- Nanassy et al. 2010 Fertil Steril 93:579-585
- Guo et al. 2014 Int J Clin Exp Path. 7(9):6191-8
- Kasterstein E. 2013 J Asst Reprod Genet 30(8):1073-9

Human Reproduction, Vol.24, No.2 pp. 300–307, 2009
Advanced Access publication on October 16, 2008 doi:10.1093/humrep/den368

human reproduction ORIGINAL ARTICLE *Embryology*

A controlled randomized trial evaluating the effect of lowered incubator oxygen tension on live births in a predominantly blastocyst transfer program†

Marius Meintjes[1,3], Samuel J. Chantilis[2], James D. Douglas[2], Alfred J. Rodriguez[2], Ali R. G[illegible]rami[2], David M. Bookout[2], Brian D. Barnett[2], [illegible] Jam[illegible] Madd[illegible][1]



Low oxygen Days 1 – 5/6

Parameter	21% Oxygen	5% Oxygen	P-value[a]
Implantation rate	95/267 (35.6%)	122/247 (49.4%)	0.003
Live-birth implantation rate	82/267 (30.7%)	106/247 (42.9%)	0.005
Clinical pregnancy rate	56/115 (48.7%)	74/115 (64.3%)	0.027
Live birth rate	49/115 (42.6%)	66/115 (57.4%)	0.043

Human Reproduction Update, Vol.19, No.3 pp. 209, 2013
Advanced Access publication on February 1, 2013 doi:10.1093/humupd/dms055

human reproduction update — IN A NUTSHELL

Low oxygen concentrations for embryo culture in assisted reproductive technologies

Back[illegible]ound — Re[illegible]

During

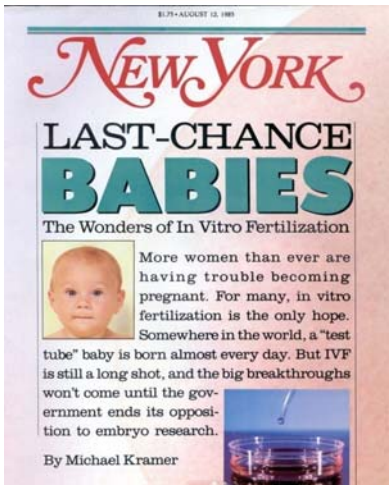
Conclusions

The results of this systematic review and meta-analysis suggest that culturing embryos under low oxygen concentrations improves the success rates of IVF/ICSI, resulting in an increase in the live birth rate.

In Vitro Culture Platforms

"small microdrops were used for culture, and enlarged when the embryos were eight celled. The embryos were left undisturbed for long periods after this time" ***Steptoe et al. 1971, Nature***

"culture with medium in a multidish under 5% CO_2 in air at 37°C in an open system"
Feichtinger et al. 1983 Acta Eur Fertil


NEW YORK

LAST-CHANCE BABIES

The Wonders of In Vitro Fertilization

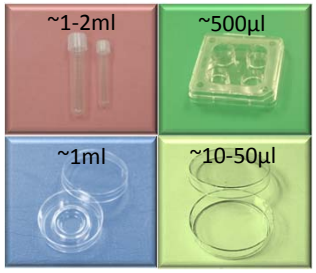
More women than ever are having trouble becoming pregnant. For many, in vitro fertilization is the only hope. Somewhere in the world, a "test tube" baby is born almost every day. But IVF is still a long shot, and the big breakthroughs won't come until the government ends its opposition to embryo research.

By Michael Kramer

As we gain tools to better understand embryo physiology, we should modify the in vitro environment to better suit their needs – this includes the culture platform (physical culture environment)

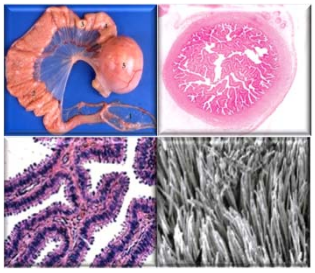
Culture Platform Comparison

In Vitro



vs.

In Vivo

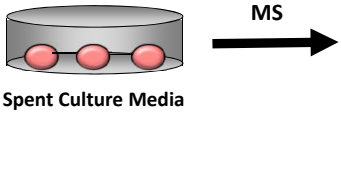


- Large volume
- Static
- Inert surfaces

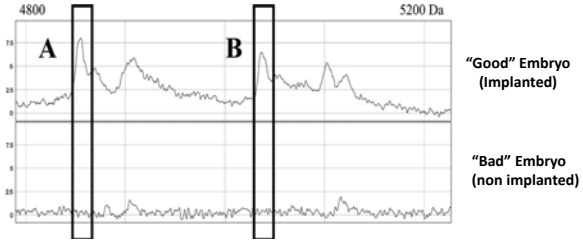
- Moist/constricted
- Dynamic
- Surface coatings

Embryo Secreted Factors (Human)

Secretome



MS



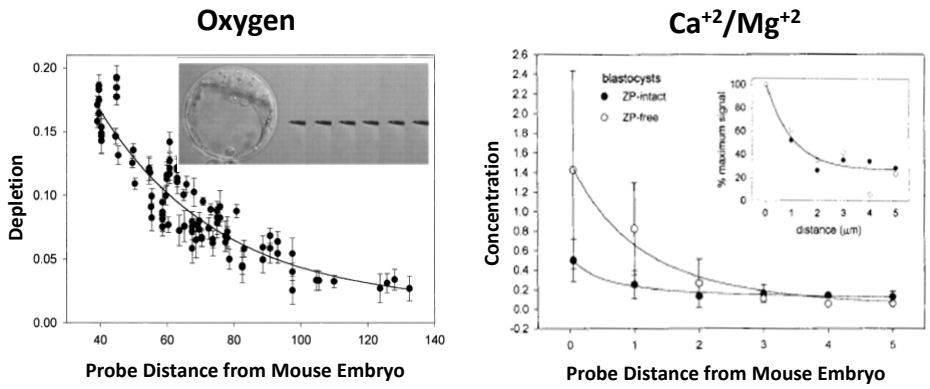
Positive Markers

CRH	(Katz-Jaffe et al. 2010)
ApoA1	(Mains et al. 2011)
Ubiquitin	(Katz-Jaffe et al. 2006)
PRC2	(Cortezzi et al. 2011)

Negative Markers

Lipocalin-1	(McReynolds et al. 2011)
TSGA10	(Cortezzi et al. 2011)

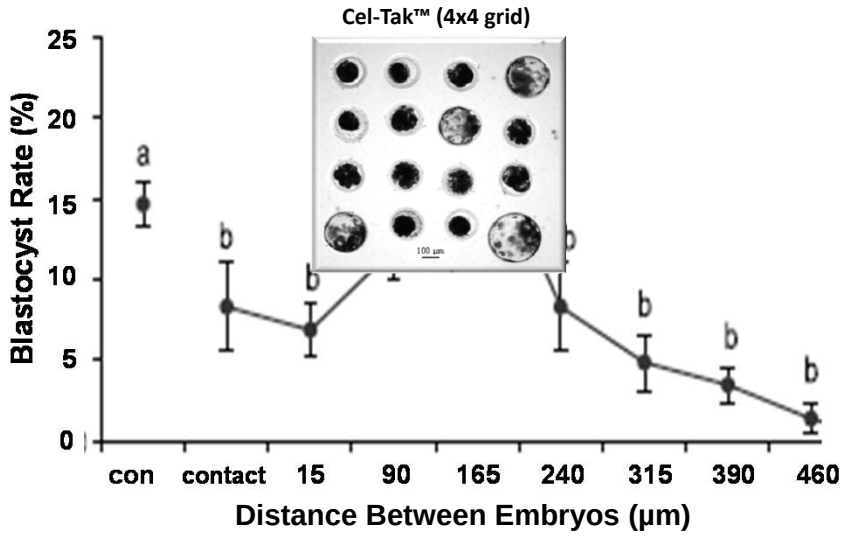
Depletion/Secretion



Embryos modify their surrounding environment
Gradients are formed

Trimarchi et al. 2000a,b

Embryo Spacing (Bovine)



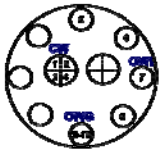
Gopichandran & Leese 2006

Benefit of Group Embryo Culture

Species	Reference	Optimal Embryo #	Volume (µl)	Embryo Density (embryo/ul)
Mouse	Wiley et al. 1986	20	10-12	**0.5-0.6**
	Paria & Day 1990	5-10	25-50	**2.5-10**
	Canseco et al. 1992	5	10	**2**
	Lane & Gardner 1992	2-16	5-320	**0.3-40**
	Kato & Tsunoda 1994	20	10	**0.5**
	Salahuddin et al. 1995	10	20	**2**
Cow	Donnay et al. 1997	20	20	**1**
	Larson & Kubisch 1999	40	25	**0.6**
	Nagao et al. 2008	25-100	50	**0.5-2**
	Ferry et al. 1994	40	40	**1**
Cat	Spindler et al. 2006	10	20	**2**
Hamster	Schini & Bavister 1988	2	<1	**<0.5**
Sheep	Gardner et al. 1994	2-4	20	**5-10**

Group Culture Effect (Human)

- Group embryo culture appears beneficial for human embryos
  Moessner & Dodson, 1995, Almagor et al., 1996, Rebollar-Lazaro & Matson, 2010
- Likely requires extended culture
- Optimal embryo density remains unknown



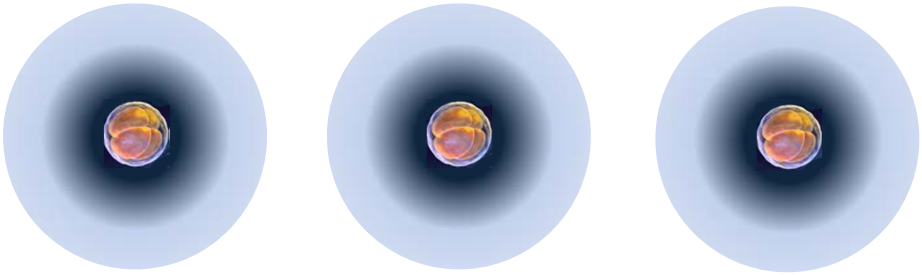
Endpoint	Center Well Group (CW)	Outer Well Individual (OWI)	Outer Well Group (OWG)
Early Compaction	38.2%[a]	38.9%[a]	**49.5%[b]**
Total Blastocyst	40.8%[a]	45.2%[a]	**55.8%[b]**
High Quality Blast	68.8%[ab]	64.7%[a]	**79.2%[b]**
Clinical Pregnancy	41.7%	38.5%	62.2%
Live Birth	41.7%	38.5%	62.2%

* Significant difference within an endpoint, p<0.05

Ebner et al. 2010

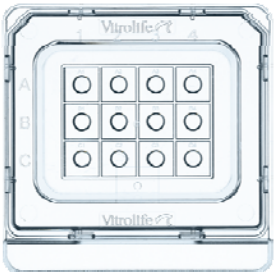
Thinking Big by Thinking Small

- Customized culture devices can create a confined culture area/volume that regulate embryo density and spacing and produce/regulate a **microenvironment** that may benefit embryo development

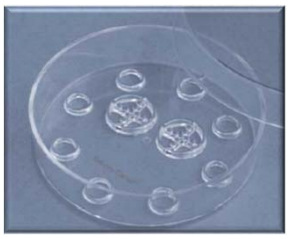


Embryo-Specific Dishes

- Rounded bottoms/edges for easy location
  - Rapid identification, embryo spacing
- Prevent microdrop dispersion or displacement



Microdroplet Dish



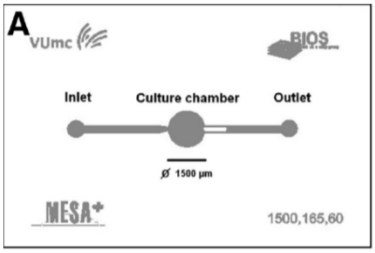
Embryo Corral®

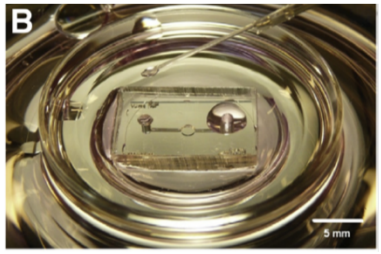
Embryo GPS®

In vitro development of donated frozen-thawed human embryos in a prototype static microfluidic device: a randomized controlled trial

Dorit C. Kieslinger, M.Sc.,[a] Zhenxia Hao, Ph.D.,[b,c] Carlijn G. Vergouw, Ph.D.,[a] Elisabeth H. Kostelijk, Ph.D.,[a] Cornelis B. Lambalk, Ph.D.,[a] and Séverine Le Gac, Ph.D.[b]

[a] IVF Center, Department of Obstetrics and Gynecology, VU University Med[illegible]nter, A[illegible]erdam, the Netherland[s]; [b] BIOS Lab on a Chip Group, MESA+ Institute for Nanotechn[illegible]gy and MIRA [illegible]; [c] Bi[illegible]; Medicine, Univers[illegible]f Tw[illegible]e, Enschede, th[illegible]lands; and [illegible] Agricultural Scie[illegible]; [illegible]eop[illegible]s R[illegible]ubli[illegible]





RBM Online - Vol 17 No 1. 2008 73-81 Reproductive BioMedicine Online; www.rbmonline.com/Article/3282 on web 28 May 2008

Article

The Well-of-the-Well system: an efficient approach to improve embryo development

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Dr Gábor Vajta

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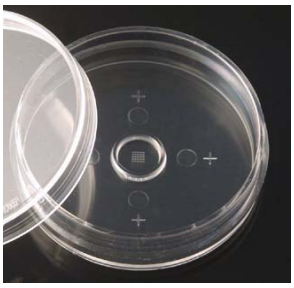
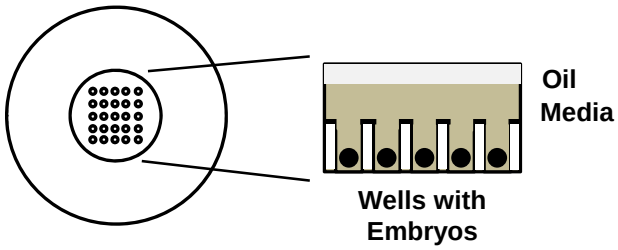
Abstr[illegible]

Well-of-the-Well (WOW)

- Constrictive – microenvironments
- Surface area/points of contact
- Permits individual ID with group effect
- Can regulate embryo spacing

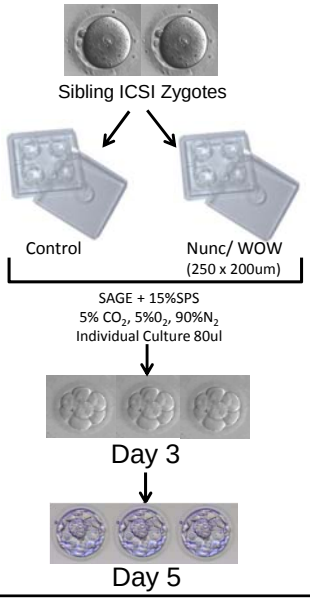


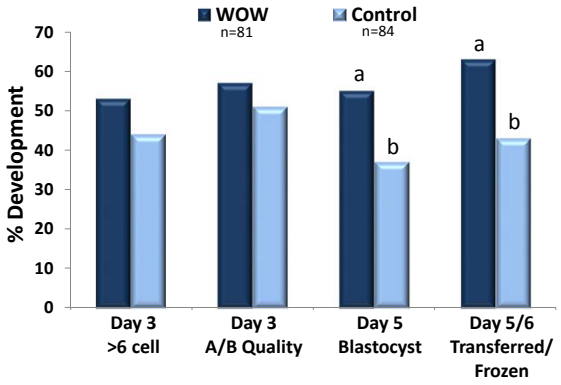


Well-of-the-Well (WOW)

Species	Well Size (*w* × *h*)	Conditions (Test vs. Con)	Endpoint (From 1-cell)	Outcome (Test vs. Con)	Reference
Bovine	700 × 700µm	1 embryo/WOW (16 total) /500µl 16 embryos/500µl µdrop (CR1aa media)	Blast @192h Blast Cell# Apoptosis	31 vs. 22% (p<0.05) 99.6 vs. 99.3 (NS) 2.8 vs. 2.6% (NS)	Hoelker et al., 2009
	287 × 168µm	1 embryo/WOW (25 total) /125µl 25 embryos/125µl µdrop (CR1aa media)	Blast @168h Blast Cell# Apoptosis Pregnancy (30d)	37 vs. 36% (NS) 111.5 vs. 102.7 (NS) 9.0 vs 13.5% (p<0.05) 51.7 vs. 25% (p<0.05)	Sugimura et al., 2010
	346 × 200µm	1 embryo/WOW (20 total) /100µl 20 embryos/100µl µdrop (IVD101 media)	Blast @192h Blast Cell#	17% vs. 18% (NS) 81.4 vs. 84.5 (NS)	Akagi et al., 2010
	1000 × 700µm	1 embryo/WOW (20total) /100µl 20 embryos/100µl µdrop (SOF media)	Blast @168h	37 vs. 30% (NS)	Matoba et al., 2010
Porcine	1000 × 300µm	4-5 embryo/WOW (3 total) /500µl 12-15 embryos/30µl µdrop (PZM3 media)	Blast @192h Blast Cell#	25 vs. 13% (p<0.05) 36 vs. 37 (NS)	Taka et al., 2005
Murine	250 × 200µm	1 embryo/WOW (5 total) /400µl 1 embryo/35µl µdrop (CZB media)	Exp Blast @144h	80 vs. 40% (p<0.05)	Vajta, 2008

WOW (Human)





Use of the WOW approach in a separate case control study of prior failed IVF patients yielded a 48.9% clinical pregnancy rate and a 37% implantation rate.

Vajta et al. 2006

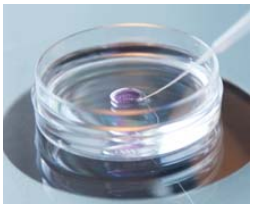
Cameras & Culture Dishes

Eeva™

Primo Vision™

Eeva dish

WOW



Platforms & Incubators

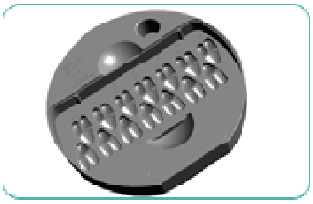
EmbryoScope™

Miri TL®

Genea Geri™

EmbryoSlide™

CultureCoin

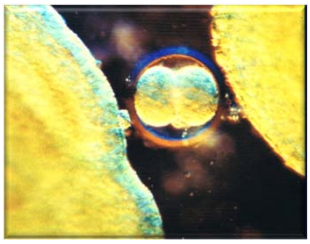


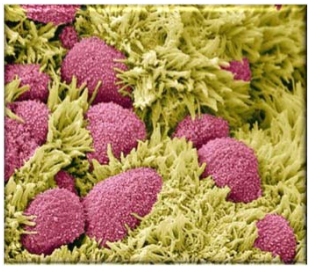
Modern Incubators

- Cleaner atmosphere
  - recirculating UV or charcoal filter units
- Faster gas equilibration
  - Smaller volume, individual chambers
- Faster temp recovery
  - Direct heat

Dynamic Embryo Culture

- *In vivo* – cilia and peristaltic muscle contractions
  - Beating frequency of 5-20Hz (Paltiel et al. 1995, Westrom et al. 1977)
  - Average speed ~0.1µm/s (Greenwald 1961)
  - Sheer force ~0-3dyn/mm^2





Gentle movement may be "normal" for embryos

"Rock-a-Bye-Baby"

Possible Benefits of Dynamic Culture

1) Disruption of gradients

- Substrate renewal?
- Removal of harmful byproducts?

Not that simple

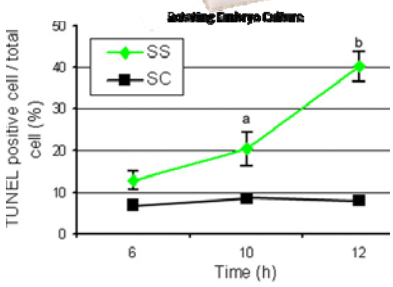
What about benefit of static micro-culture?

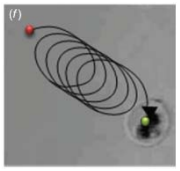
2) Mechanical stimulation

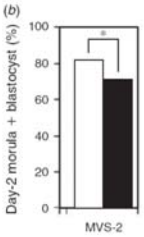
- Sensory mechanotransduction (Synthichaki & Tavernarakis 2003)
  - Cell ability to respond to physical stimuli
  - Influences ion channels, etc
- Possible activation of trophic signaling pathways

"Don't Shake the Baby"

- Mouse embryos can sense sheer stress
  (Xie et la. 2006, 2007, Asano & Matsuura 2014)
  - >1.2dyn/cm^2 induces apoptosis







Active Embryo Hypothesis

- Excessive movement and resulting sheer forces can be detrimental to embryo development, activating signaling pathways that lead to apoptosis. Less vigorous or periodic movement or other physical stimuli, such as surface interactions, vibrations or gentle media flow, can be embryo-trophic.

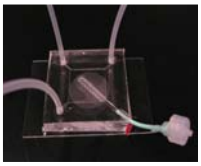
Early Attempts at Dynamic Culture

- Orbital shakers (Zeilmaker et al. 1971, Hoppe & Pitts 1973, Cohen 1981)

- Macroscale perfusion systems (Pruitt et al. 1991, Lim et al. 1996, Thompson et al. 1997)

- Microchannel perfusion (Hickman et al. 2002)
  - Gravity
  - External pumps
  - Cell recovery

- Perfusion co-culture (Mizuno et al.2007)
  - External pumps
  - Cell recovery



Technical limitations to early systems

Dynamic Culture

- Dynamic embryo culture appears beneficial
- May be a role for periodic physical stimuli
  - Constant movement not required
- Still need to optimize dynamic conditions
  - Speed, duration, motion paths, embryo density
- Need a refined **system** for widespread clinical use
  - static culture is still the "norm"

Isachenko et al. 2010, 2011
Hur et al. 2013

Vibrating

Matsuura et al. 2010
Hara et al. 2013

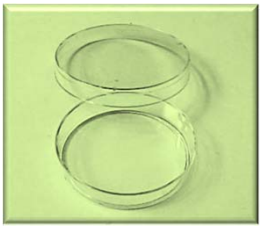
Tilting

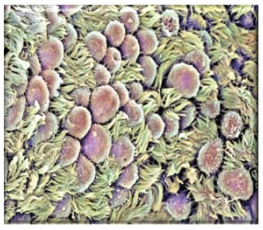
Heo et al. 2010
Algreti et al. 2011

Microfluidic Pulsative Flow

Culture Surfaces

In Vitro ***In Vivo***

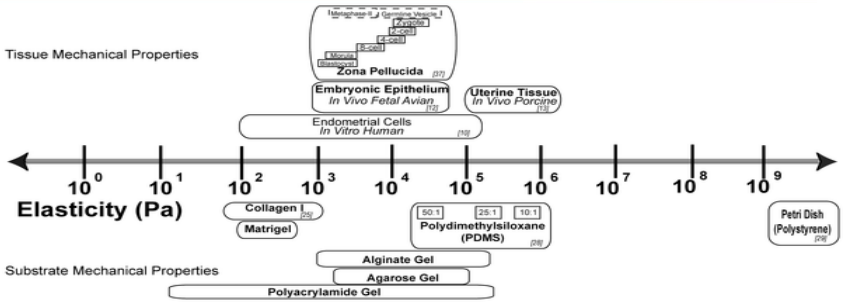




- Some polymers can be detrimental to embryo development (Hunter et al. 1988)
- Polystyrene dishes may compromise growth of adherent cells (Summer et al. 2012)
  - Softens under water
  - Alters microenvironment
    - pH increase at interface, generation of ROS

Could a novel surface/material improve embryo development?

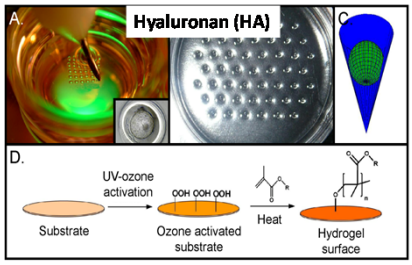
Culture Surfaces

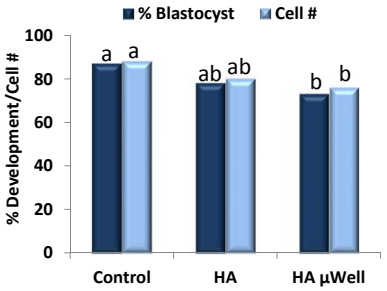


- Reduced "stiffness" of collagen and PDMS surface improved mouse embryo development (Kolahi et al. 2012)
  - What about the zona barrier?
  - Perhaps more likely a result of absorption/alteration in media composition?
    - PDMS can leach, absorb and change media osmolality (Heo et al. 2012, Regeher et al. 2009, Toepke & Beebe 2006)

Surface Coatings

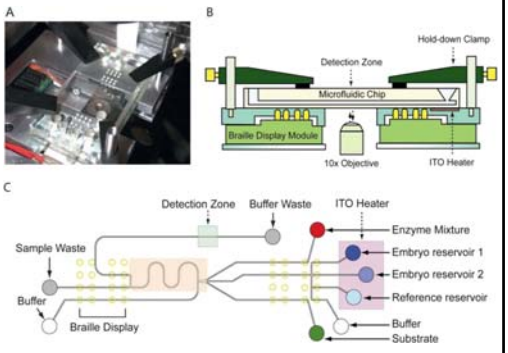
- Matrigel coating can be beneficial or detrimental to mouse embryo development
  (Dawson et al. 1997, Lazzaroni et a. 1999, Carnegie et al. 1995)
  - Strain specific?
- Agarose has been used to culture zona free embryos
  (Brandao, et al. 2004, Peura & Vajta 2003)
  - No specific benefit noted
- Hyaluronan coating was detrimental to mouse embryo development when used for microwells (Oakes et al. 2009)





An Ideal Culture Platform?

- Individually housed micro-culture/dynamic platforms
  - no need for daily opening and dish removal
  - permit group culture with individual ID
- Real-time imaging
  - vibrating camera, etc
- Inline Assays/Measures
- Specialized material/surface
  - Growth improvement
  - Protective (light filtering, etc)
- Customized media exchange?
- **USER FRIENDLY**
- **AFFORDABLE**



Heo et al. 2012

Is this feasible?

Chemical Atmosphere/Platform

Abstracts of the 26th Annual Meeting of ESHRE, Rome, Italy, 27 June – 30 June, 2010

O-108 A self-contained culture platform utilizing chemically generated carbon dioxide supports mouse blastocyst development in vitro

J. Swain[1]

[1]*University of Michigan, Obstetrics & Gynecology, Ann Arbor MI, U*

Journal of Reproduction and Development, Vol. 57, No. 4, 2011

—Technology Report—

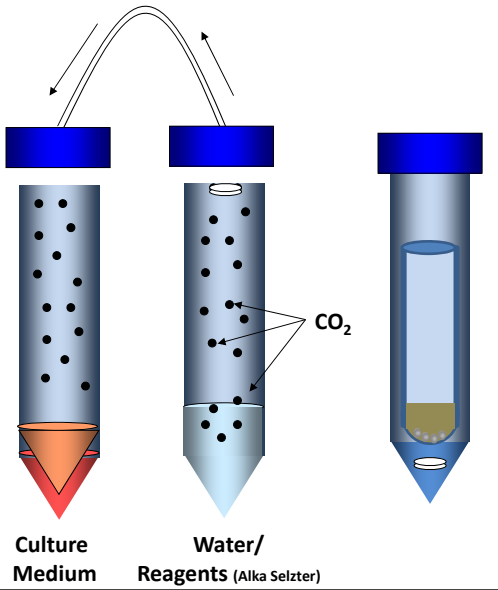
A Self-Contained Culture Platform Using Carbon Dioxide Produced from a Chemical Reaction Supports Mouse Blastocyst Development *In Vitro*

Jason E. SWAIN[1)]

[1)]*Department of OB/GYN, Reproductive Sciences Program, University of Michigan, MI 48*

Abstract Elevat… CO_2 is required for *in vitro* embryo culture to maintain p… …lternative to current a… …paches usi… …ga…

Chemical Atmosphere/Platform



-no need for a gas incubator

-provides a stable pH

-clean gas supply

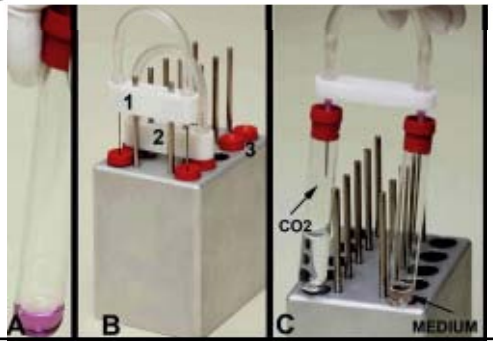
Reproductive BioMedicine Online (2014) 28, 310–320

www.sciencedirect.com
www.rbmonline.com

ARTICLE

First births with a simplified culture system for clinical IVF and embryo transfer

Jonathan Van Blerkom[a,b,*] ...



In Vivo Culture

INVO Cell

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

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Home > Find Studies > Study Record Detail

Vaginal Culture Using INVOcell Compared to Traditional IVF Incubation

This study is currently recruiting participants. (see Contacts and Locations)
Verified February 2015 by Invaron Pharmaceuticals Inc.

Sponsor:
Invaron Pharmaceuticals Inc.

Information provided by (Responsible Party):
Invaron Pharmaceuticals Inc.

ClinicalTrials.gov Identifier:
NCT02363426

First received: February 5, 2015
Last updated: February 9, 2015
Last verified: February 2015
History of Changes

In Vivo Culture

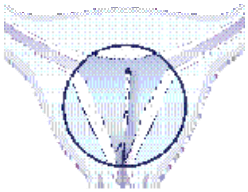
Human Reproduction, Vol.24, No.4 pp. 790–796, 2009
Advanced Access publication on March 10, 2009 doi:10.1093/humrep/dep005

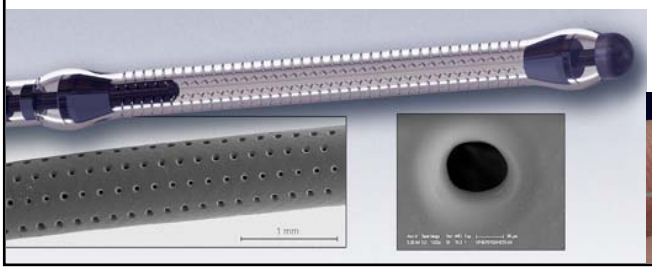
human reproduction ORIGINAL ARTICLE *Embryology*

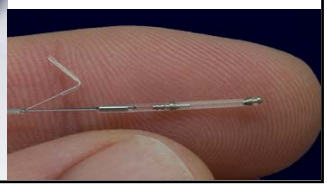
An *in vivo* culture system for human embryos using an encapsulation technology: a pilot study

C. Blockeel[1,†], P. Mock[2,9,†], G. Verheyen[1,†], N. Bouche[2,3], Ph. Le Goff[2], Y. Heyman[4], C. Wrenzycki[5], K. Höffmann[5], H. Niemann[6], P. Haentjens[7], M.J. de Los Santos[8], M. Fernandez-Sanchez[8], M. Velasco[2], P. Aebischer[3], P. Devroey[1], and C. Simón[8,10]

ANECOVA-D







Conclusions

- Numerous procedural steps involved in IVF
  - All carry potential for cellular stress
- Conditions should be customized for the changing physiology of the respective cell types/stages in each of these steps
- Many variables to consider other than simply selecting culture media
- **Consistency**- knowledge, oversite & QC is essential

Acknowledgements

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Colorado Center for Reproductive Medicine
Making Dreams Conceivable

NATIONAL FOUNDATION FOR
Fertility Research

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