Knowing Where We Came From: History of Clinical IVF

Thomas B. Pool, Ph.D., HCLD
Fertility Center of San Antonio
San Antonio, Texas

Disclosures

“The vast majority of human beings dislike and even actually dread all notions with which they are not familiar…Hence, it comes about that at their first appearance, innovators have generally been persecuted, and always, derided as fools and madmen.”

Aldous Huxley
author
***Brave New World*, 1932**

“Most human beings have an almost infinite capacity for taking things for granted”.

Acknowledgements

I want to thank the following individuals for their altruism and assistance in preparing this presentation for the College of Reproductive Biology:

Peter Brinsden (l) with James Watson and Bob Edwards

Lucinda Veeck Gosden

KAY ELDER

Loretto Senior In Recital

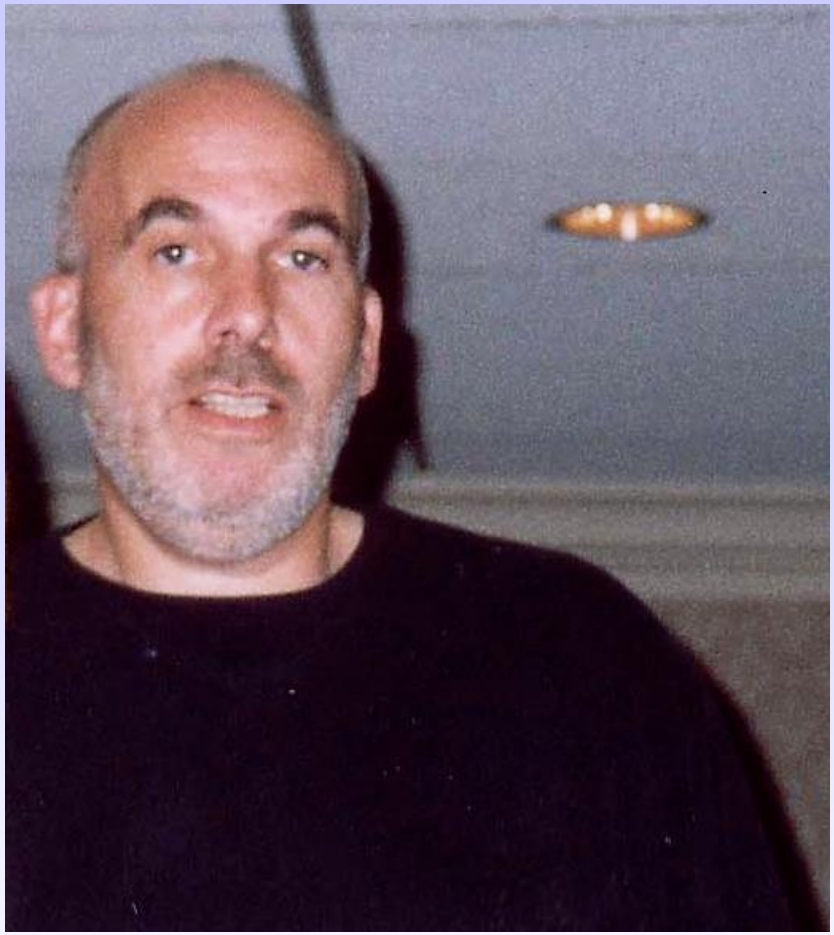
Music Department of Loretto Academy will present Miss Kay Elder in senior piano recital at 7:30 p.m. May 30 in the Little Theater. The public is invited.

Miss Elder, daughter of Mr. and Mrs. Frank A. Elder of Forest, Chihuahua, Mexico, She has been a student at Notre Lady Heights for the past four years and has served as accompanist for the voice department, glee club and orchestra. Her program is as follows:

French Suite No 5 in
G Major ..... Bach
Gavotte — Gigue.
Sonata, Op. 2, No. 1 Beethoven
Prestissimo.
Impromptu in A Flat,
Op. 90, No. 4 ..... Schubert
Elegie, Op. 3,
No. 1 .....Rachmaninoff
Minstrels .....Debussy
O Primitivels ... H. Villa-Lobos
Waltz, Op. 64, No. 2 ....Chopin
Prelude, Op. 28, No. 15...Chopin
Waltz, Op. 34 .....Chopin

Kay Elder

Professor Sir Richard L. Gardner



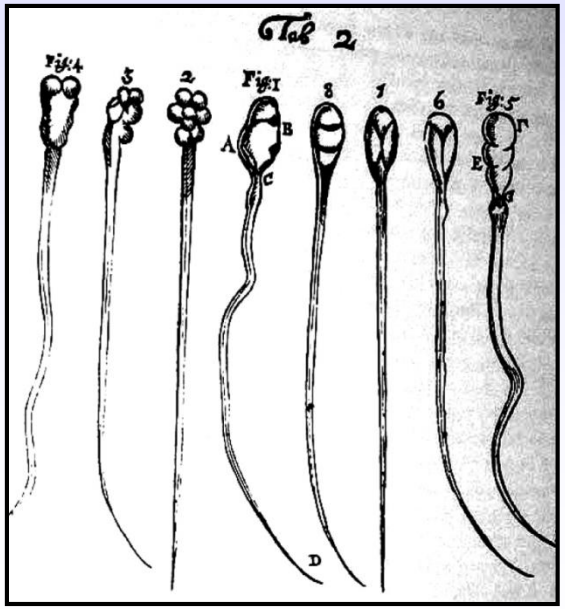
Jacques Cohen

Cohen, Jacques, 2013. From Pythagoras and Aristotle to Boveri and Edwards: a history of clinical embryology and therapeutic IVF. In: *Textbook of Clinical Embryology* (Coward K., Wells, D.,eds) Cambridge University Press, p177-102.

Henry Leese

The early history of IVF 1

- Aristotle (384-322 BC) proposed the theory that children are a product of "the mingling of male and female seed". This opposed the prevailing theory that children were from the male seed and women merely the "receptacle for the child".
- William Harvey (1578-1657) studied the fertility of the King's herd of deer, and wrote: "De generatione animalium" in1651, in which occurs the well known phrase: "Ex ovo omnia" – "from the egg is everything".
- Antonj van Leeuwenhoek (1632-1723) carried out the first studies on human sperm with the newly invented microscope.
- Report of homunculus (miniature human within a sperm) by Dalenpatius (1699) turns out to be a hoax!



Van Leeuwenhoek's drawings of sperm

The early history of IVF

- Spallanzani (1729-1799), an Italian Scientist, studied semen in mammals. He performed artificial insemination (AI) in a spaniel bitch – the first recorded instance of AI. He is also credited with the first freezing of sperm in 1776.
- John Hunter in c.1790 performed the first successful human AI for a man with hypospadias.
- Carl Ernst von Baer (1792-1876). In 1826 he identified mammalian oocytes in the ovaries of a bitch. He is credited with being "the father of modern embryology".
- Henry Nelson (1852), Newport (1853), van Beneden (1854) and Hertwig (1876) all report observing the process of fertilization in ascaris, amphibians and mammals, respectively.

Carl von Baer

The early history of IVF

- Theodor Boveri (1880's – 1912)

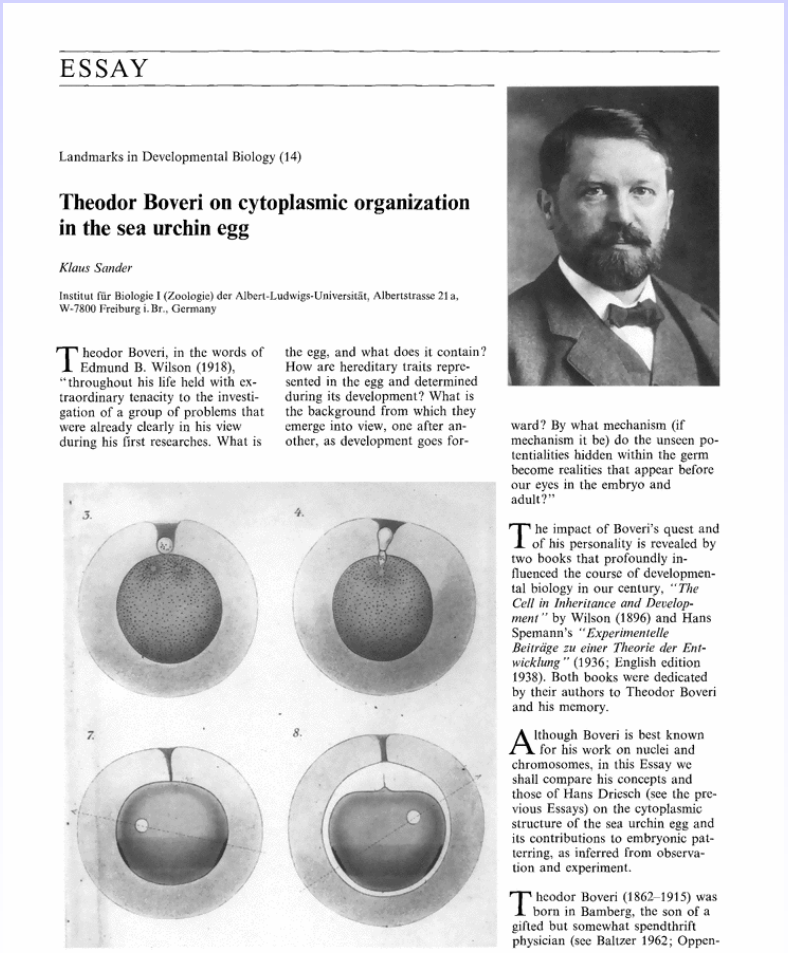
Reduction of chromosome number during egg maturation.

Along with Sutton, advanced the chromosome model of inheritance.

Discovered the centriole.

Nominated for Nobel Prize.

Work done with *Ascaris* and sea urchins; Sutton, with grasshoppers.



ESSAY

Landmarks in Developmental Biology (14)

Theodor Boveri on cytoplasmic organization in the sea urchin egg

Klaus Sander

Institut für Biologie I (Zoologie) der Albert-Ludwigs-Universität, Albertstrasse 21a, W-7800 Freiburg i.Br., Germany

Theodor Boveri, in the words of Edmund B. Wilson (1918), "throughout his life held with extraordinary tenacity to the investigation of a group of problems that were already clearly in his view during his first researches. What is the egg, and what does it contain? How are hereditary traits represented in the egg and determined during its development? What is the background from which they emerge into view, one after another, as development goes forward? By what mechanism (if mechanism it be) do the unseen potentialities hidden within the germ become realities that appear before our eyes in the embryo and adult?"

The impact of Boveri's quest and of his personality is revealed by two books that profoundly influenced the course of developmental biology in our century, *"The Cell in Inheritance and Development"* by Wilson (1896) and Hans Spemann's *"Experimentelle Beiträge zu einer Theorie der Entwicklung"* (1936; English edition 1938). Both books were dedicated by their authors to Theodor Boveri and his memory.

Although Boveri is best known for his work on nuclei and chromosomes, in this Essay we shall compare his concepts and those of Hans Driesch (see the previous Essays) on the cytoplasmic structure of the sea urchin egg and its contributions to embryonic patterning, as inferred from observation and experiment.

Theodor Boveri (1862–1915) was born in Bamberg, the son of a gifted but somewhat spendthrift physician (see Baltzer 1962; Oppen-

The early history of IVF

- Walter Heape (c. 1890) of Cambridge, UK, transplanted embryos into rabbits.

Angora rabbit – embryo donor.

Belgian hare - recipient

Embryos were washed from the oviducts and transferred to the recipient with little laboratory exposure – first transfer of a "segmented ova" (cleaved embryo).

Siblings were mixed as the Belgian had been bred.

Of interest, experiments were performed either in his laboratory in Cambridge or in Prestwick near Manchester, his home – parallels the trek of Bob Edwards during the pioneering days of human IVF with Steptoe.

The early years of human IVF 1

Events leading to human IVF:

- Pincus and Enzman (1934) propose that human oocytes could develop normally *in vitro*.
- Dr. John Rock (1937) suggested “ectogenesis”as a means of treating tubal disease in women.
- M.F. Menkin and J. Rock (1948) attempt *in vitro* fertilization of human oocytes with modest results
- Polge (1949) reports the first practical freezing of animal spermatozoa using glycerol.
- Chang and Austin (1951) independently identify capacitation.
- McLaren and Biggers (1958) produced young from the transfer of blastocysts grown in Whitten’s medium to recipient mouse.
- Chang (1959) performs successful IVF in the rabbit.

Some major events and findings in the history of IVF*

384-322 BC Aristotle writes the first account of embryology
1561 Fallopius provides first correct anatomical description of the Fallopian tube
1677 Discovery of mammalian spermatozoa: A van Leeuwenhoek
1797 Recovery of embryos from rabbit Fallopian tube: W C Cruikshank
1827 Identification of an egg in a mammalian ovarian follice: von Baer
1878 Understanding that fertilisation requires the fusion of one sperm with one egg: Hertwik (sea urchin), Van Beneden (rabbit) & Fol (starfish)
1890 First embryo transfer (in rabbit) W. Heape
1912 First culture of mammalian embryos: Brachet
1930 First experiments on IVF (rabbits): Pincus
1932 Publication of *Brave New World*: A Huxley
1944 First attempt at IVF using human oocytes: Rock & Menkin
1949 Culture medium in which 8 cell mouse embryos developed to blastocysts J Hammond Jr
1951 Capacitation in sperm: Chang : Austin
1958 Transfer of cultured mouse blastocyst to the uterus of another female followed by birth of live young (McLaren & Biggers)
1959 Unequivocal demonstration of IVF in the rabbit (Chang)
1969 Demonstration of human oocyte fertilisation in vitro: Edwards, Bavister & Steptoe
1972 Successful freezing of mammalian embryos (mouse): Wilmut : Whittingham
1976 First human pregnancy (ectopic) after IVF and embryo transfer: Steptoe & Edwards
1978 Birth of first child following IVF and embryo transfer: Steptoe & Edwards

*courtesy of Henry Leese

The Development of Human IVF

Father of *In Vitro* Fertilization, Bob Edwards

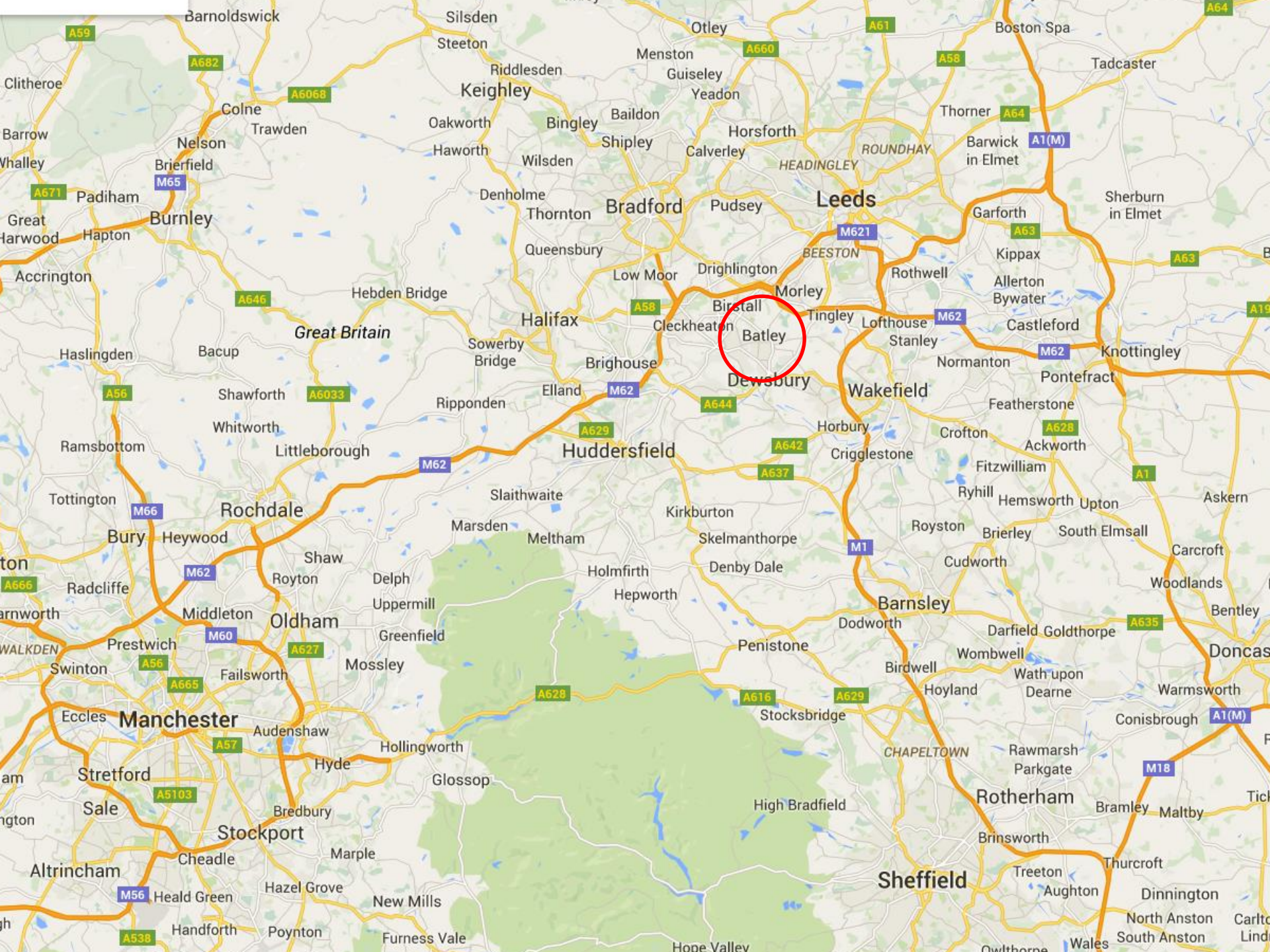
Bob with Kay Elder, Bourn Hall, Louise Brown's 30th birthday party, 2008

SIR ROBERT GEOFFREY EDWARDS C.B.E

27 September 1925 – 10 April 2013

Elected F.R.S 1984

By SIR RICHARD GARDNER F.R.S
Department of Biology, University of York,
York, YO10 5YW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Burnley
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Accrington
Low Moor
Drighlington
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Allerton Bywater
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Elland
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Featherstone
Whitworth
Horbury
Crofton
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Ramsbottom
Littleborough
Huddersfield
Crigglestone
Fitzwilliam
Slaithwaite
Ryhill
Hemsworth
Upton
Askern
Tottington
Rochdale
Kirkburton
Royston
Brierley
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Bury
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Meltham
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Carcroft
Shaw
Holmfirth
Denby Dale
Cudworth
Radcliffe
Royton
Delph
Hepworth
Woodlands
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Dodworth
Darfield
Goldthorpe
Bentley
Greenfield
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Prestwich
Wombwell
Doncas
Swinton
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Hollingworth
Hyde
Parkgate
Stretford
Glossop
Rotherham
Sale
High Bradfield
Bramley
Maltby
Bredbury
Brinsworth
Stockport
Cheadle
Marple
Thurcroft
Altrincham
Treeton
Sheffield
Hazel Grove
Aughton
Dinnington
Heald Green
New Mills
North Anston
Handforth
Poynton
Furness Vale
South Anston
Hope Valley
Wales

Bob Edwards – the early years

- Born in 1925 in Batley to Samuel, an engineer's laborer and Margaret Edwards, a machinist

- Two brothers, Samuel and Harry Raymond

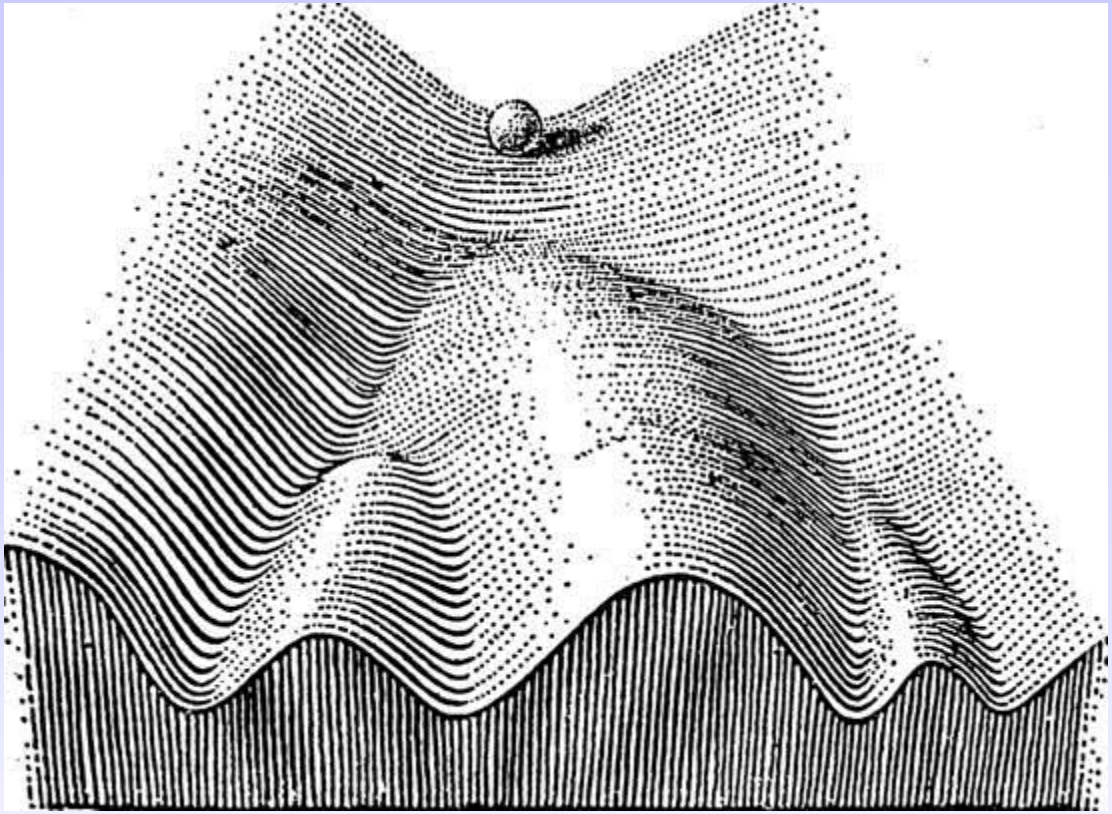
- Local school evacuated to Blackpool due to WWII but returned home in 6 mos. – hiatus from school put him into agriculture

- Entered Army in 1943 – instructor in driving tracked vehicles

- 1948, entered University College of North Wales studying agriculture but lost interest and turned to zoology (Zoology was headed by F.W. Rogers Brambell, FRS 1949).

- Accepted to Edinburgh but took menial jobs to pay for first three months (harvest laborer, dock laborer unloading bananas, hauled heavy flour sacks at mills, office boy at newspaper)

Conrad Hal Waddington
(1905-1975)



C.H. Waddington, FRS 1947
Head – Institute of Animal Genetics
Edinburgh University

•Bob performed well in the Postgraduate Diploma course and Waddington invited him to stay for his Ph.D.

•Studied the modification of chromosomal complement of the mouse embryo under Dr. Alan Beatty

•Made numerous observations of the timing of the events of oocyte maturation, fertilization and early embryonic development under normal and abnormal chromosomal conditions

•Tutored postdoctoral fellow at Edinburgh, Mary Lyon, on reproductive physiology of the mouse.

- Bob met and married geneticist Ruth Fowler at while at Edinburgh in 1954. Pioneered concept of ovulation induction in the mouse.

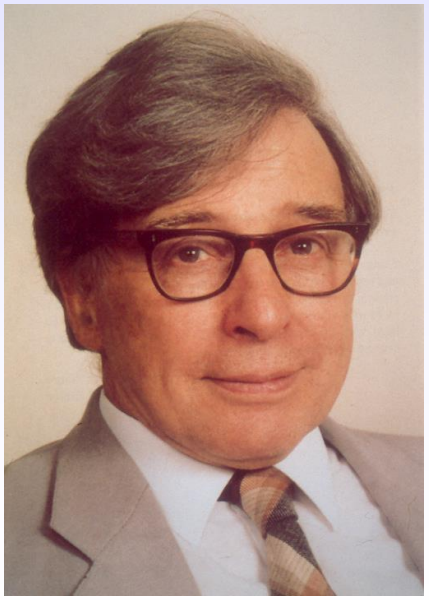
- Spent one year at Cal Tech with Albert Tyler in reproductive immunology

- Five years as a postdoctoral fellow at Mill Hill (NIMR) with Sir A.S. Parkes (FRS1933) and studied maturation in vitro of mouse, rat, hamster, etc.

- Parkes moves to Cambridge in 1961 and invites Bob to join him in 1963 – committed to fertilizing human oocytes in vitro, but no source of oocytes.

Johns Hopkins University
Baltimore 1965

- Parameters of spontaneous human meiosis
- Capacitation – the key to fertilization
  - Washed sperm (swim up)
  - Cervical mucus
  - Endometrium
  - Fallopian tube
  - Rabbit
  - Cynomolgus monkey



Howard Jones and Bob Edwards

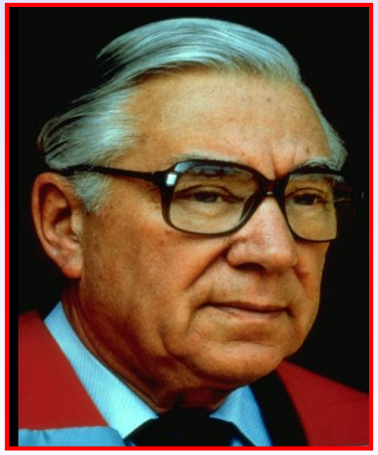
November 6, 1965 THE LANCET

MATURATION IN VITRO OF HUMAN OVARIAN OÖCYTES

R. G. EDWARDS
Ph.D. Edin., D.Sc. Wales

From the Division of Medical Genetics, School of Medicine, The Johns Hopkins Hospital, Baltimore, U.S.A., and the Physiological Laboratory, University of Cambridge *

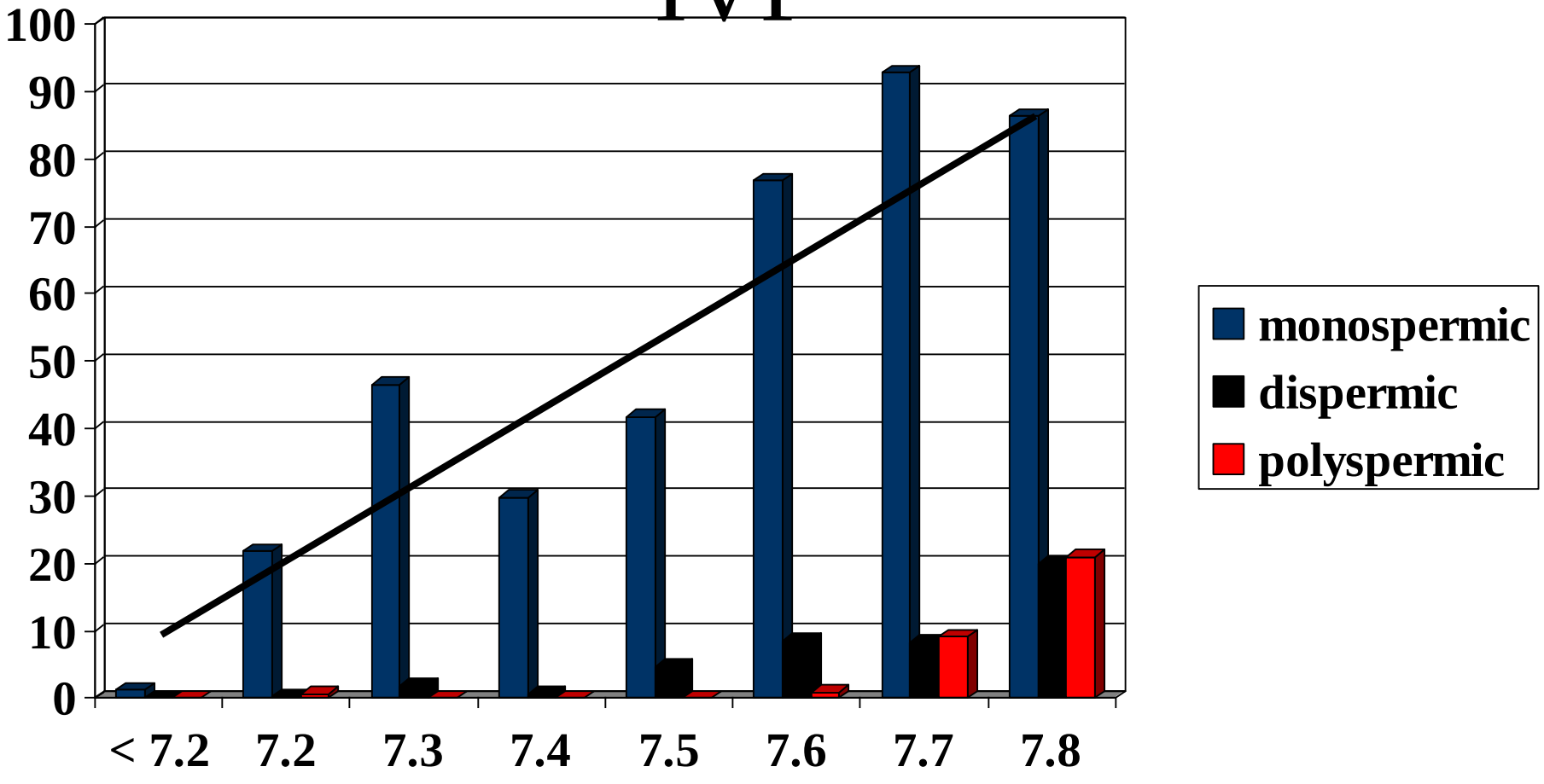
- Raoul Palmer of France, a pioneer in laparoscopy, developed a technique to collect oocytes laparoscopically in 1961. Patrick Steptoe of the UK learns this technique from Palmer.
- Edwards and Steptoe begin collaboration in 1968.



Patrick Steptoe, FRS 1987

Barry Bavister and Bob Edwards, Cambridge

pH-Dependence of Hamster IVF



Bavister 1969 *J. Reprod. Fertil.*

Final Road to Success

- In 1973, a group from Australia, led by Professors Carl Wood and John Leeton reported the first human IVF pregnancy, but it turns out to be a “biochemical pregnancy”.

- Steptoe and Edwards in 1976 announce the first clinical IVF pregnancy – but it is found to be an ectopic pregnancy.

- After 102 failed embryo transfers (ET), Steptoe and Edwards achieve the first ongoing human IVF pregnancy in Mrs Lesley Brown, who had severe tubal factor infertility.

The World's First IVF Baby is Born – 25 July 1978

On 25 July 1978, Louise Brown was born by Caesarean section at Oldham General Hospital, England – the first baby to be born as a result of IVF in a human.

TIME EXPRESS
See Page 20

EXPRESS

No. 24,281 Wednesday July 26 1978 Weather: Rainy at first 8p ★★★★

EXPRESS BABY OF THE CENTURY

Born safe—the world's first test-tube baby weighs in at 5lb 12oz and mother's delighted

IT'S A GIRL

By Harry Pugh

IT'S A GIRL! THE WORLD'S FIRST TEST-TUBE BABY WAS BORN LATE LAST NIGHT. SHE CAME INTO THE WORLD NEAR MIDNIGHT. BOTH MOTHER AND BABY ARE WELL.

There were no hitches, the mother, 32-year-old Mrs Lesley Brown, is "doing well" and the baby is perfectly formed. A living miracle weighing in at 5lb 12ozs.

The birth will bring world acclaim for Britain's medical profession, after 12 years of research.

The two men who have created life in a test tube, gynaecologist Mr Patrick Steptoe and scientist Dr Robert Edwards, were said to be "enthralled."

They had taken an egg from driver's wife Mrs Brown, fertilised it with her husband's sperm, then replanted the foetus in her womb.

Mrs Brown, childless after nine years of marriage because a fault in her fallopian tubes, had her baby in a 45-minute caesarean operation.

MAGIC MOMENT

Howard and Georgeanna Jones

7/27/78

They worked with 'test tube' scientist

Birth breakthrough thrills new EVMS profs

By JULIA WALLACE
Ledger-Star Staff Writer

NORFOLK — Two new Eastern Virginia Medical School professors who worked with a member of the English test tube baby team said today they were thrilled with the Wednesday birth.

"We're just delighted," said Dr. Howard Jones, 67, former head of the genetics lab at John Hopkins University in Baltimore. "We know how hard he had worked."

Jones and his 66-year-old wife, Georgeanna, both gynecologists, worked with Dr. Bob Edwards in Baltimore during the summer of 1966.

Edwards, a basic scientist, is on the English team based at Cambridge University.

See related stories on page A19.

Edwards did not have human eggs for research, so he came to the Jones' lab to experiment.

The Joneses said they are capable of doing the same type of research on the English team. They hope to find the funds to begin such a project.

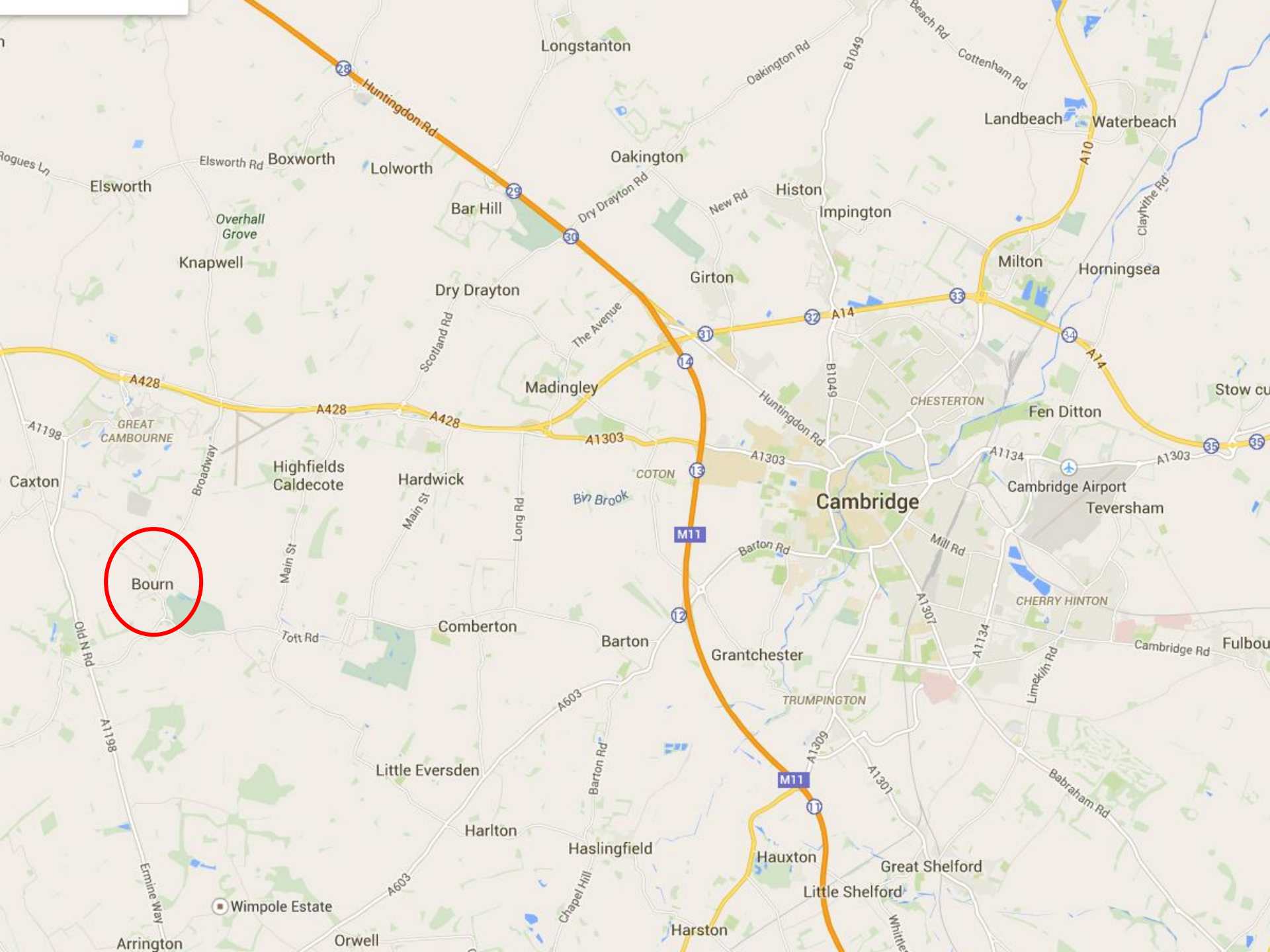
"The lab will be used for genetic diagnosis now, but test tube baby research takes place in exactly this kind of lab. It's already made for it," Howard Jones said.

In 1975, the Department of Health, Education and Welfare barred any federal funding for this type of research unless the projects are approved by the federal ethics Advisory Board. No projects yet have been approved.

Wednesday a 5-pound, 13-ounce test tube baby was born in Oldham, England, by Caesarean section. The baby is reported in good health.

The egg had been taken from the mother, Lesley Brown of Bristol, England, fertilized in a test tube for five days with the sperm of her husband, Michael, and then implanted in her uterus.

(Continued on page B9, col. 2)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Babraham Rd
Little Eversden
Barton Rd
Harlton
Haslingfield
Hauxton
Great Shelford
Little Shelford
Ermine Way
Wimpole Estate
Chapel Hill
Harston
Arrington
Orwell

Bourn Hall Clinic, Bourn, England


ALPHA
2001

Dr. Peter Robert Brinsden, MBBS, MRCS, LRCP, FRCOG

Medical Director, Bourn Hall Clinic, 1989-2006;
Consultant Medical Director, 2006-present

HONOURS AND AWARDS

Medals and Prizes

1970 Medal of the American Fertility Society
1971 Darwin Medal, Institute of Biology, UK
1973 Adair Award, American Gynecological Society
1980 Serono Prize, American Fertility Society
1985 Spanish Fertility Society Gold Medal
1987 Gold Medal, City of Toulouse, France
1988 CBE
1989 Co-winner of the King Faisal International Prize for Medicine
1991 Steptoe Memorial Medal and Prize, British Fertility Society
Marshall Medal , Society for the Study of Fertility, UK
Barbara Eck Manning Award, Resolve, USA
1994 Berthold-Gedachtnis Medal, German Society of Endocrinology
1996 Pierre Soupart Lecture, Axel Munthe Award, Naples
1998 Gold Medal, University of Sassari, Sardinia
1999 Gold Medal Award of the International Federation of Associations of Anatomists Malpighi Symposim, University of Rome
2000 Bertarelli Foundation Award in Reproductive healthcare
FIGO Recognition Award to non-Obstetricians/Gynecologists
Rotary Club Chennai " For the Sake of Honour Award"
2001 Albert Lasker Award for Clinical Medical Research
Nature Medicine Prize
2002 Distinguished Lifetime Achievement Award, Reproductive Biology Professional Group ASRM
Robert Edwards Award, American Infertility Association, New York
The Grand Hamdan International Award for Obstetrics and Gynecology (Infertility), Dubai
2003 Award of the Egyptian Ministry of Health
2004 Pioneer in Stem Cell Award, Pittsburgh Development Center
2005 Eardley Holland Gold Medal, Royal College of Obstetrics and Gynaecology, London, UK
2006 30th Joseph Bolivar DeLee Humanitarian Award, Chicago Lying-in Hospital Board of Directiors & Departement of Obstetrics and Gynecology, University of Chicago

Courtesy of Sir Richard Gardner

2007 Chevalier dans l'Ordre National de la Legion d'Honneur, Paris
Jacques Salat-Baroux Prize, Paris
Life Achievement Award, the German Society for Reproductive Medicine
2008 Pride of Britain Award- Lifetime Achievement
2010 Nobel Prize in Physiology or Medicine
2011 Knighthood

Membership of Academies, etc.

1983 Honorary Member of the French Society for Infertility
1984 Fellow of the Royal Society
1985 Founder member of the European Society for Human Reproduction and Embryology (ESHRE)
Honorary Citizen, Bordeaux, France
Life Fellow of Australian Fertility Society
Fellow ad eundem, Royal College of Obstetricians and Gynaecologists
1986 Honorary Member of the Royal College of Physicians
1988-1990 President, Ribblehead Sheep Show
Honorary President British Fertility Society
1990 Honorary Member , Pacific Coast fertility Society
1992 Honorary Fellow, German Society of Gynecology and Obstetrics
Honorary President, French Gynecological Society
Keys of San Diego City
1993 Honorary Fellow, Royal Society of Medicine
Honorary Fellow , European Society of Human Reproduction and Embryology
1995 Honorary Member, Italian Society of Anatomy
1998 Honorary Member, Association of Clinical Embryologists, UK
Honorary President , Alpha – International Society for Scientists in Reproductive Medicine
Honorary Member, Greek Fertility Society
Honorary Fellow, International Federation of Fertility Societies, San Francisco
1999 Honorary Member of the Middle East Fertility Society
Patron, UK National Gamete Donation Trust

Courtesy of Sir Richard Gardner

2000 Life membership. Indian Society for the Study of Reproduction and Fertility
2001 Honorary Membership , Society for Reproductive Endocrinology and Infertility, American Society for reproductive Medicine

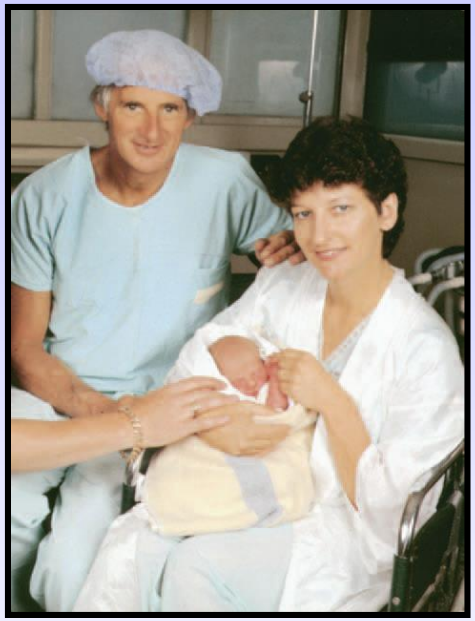
Courtesy of Sir Richard Gardner

Robert G. Edwards, September 27, 1925 – April 10, 2013

2010 Nobel Prize, Physiology or Medicine

The early years of Human IVF

- 1980. Candice Reed, the World's third IVF baby is born in Melbourne, Australia, as a result of the pioneering work of Professors Carl Wood and Alex Lopata.



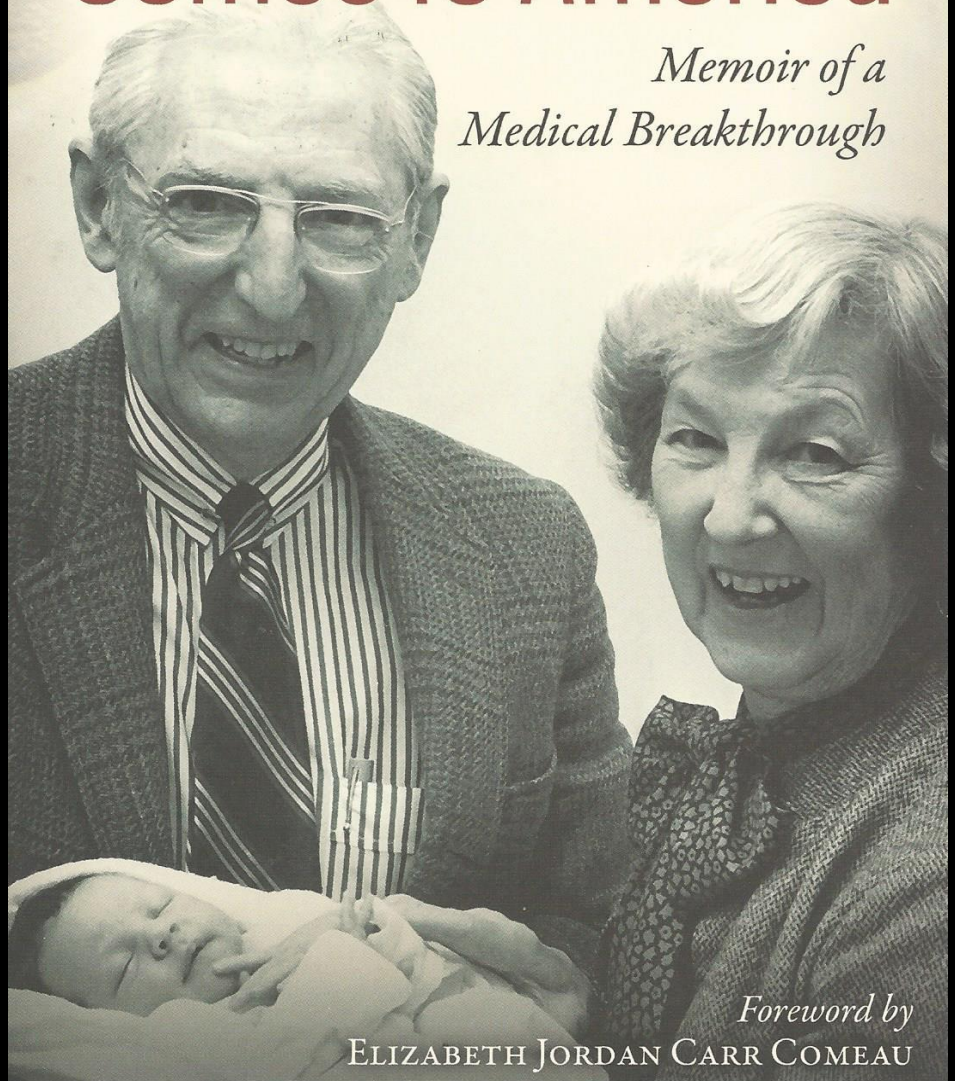
Prof. Carl Wood with Mrs. Reed and Candice

- Altruism and expertise of Dr. Alan Trounson helped new programs worldwide in the early 1980's.

Howard W. Jones, Jr., M.D.

In Vitro Fertilization Comes to America

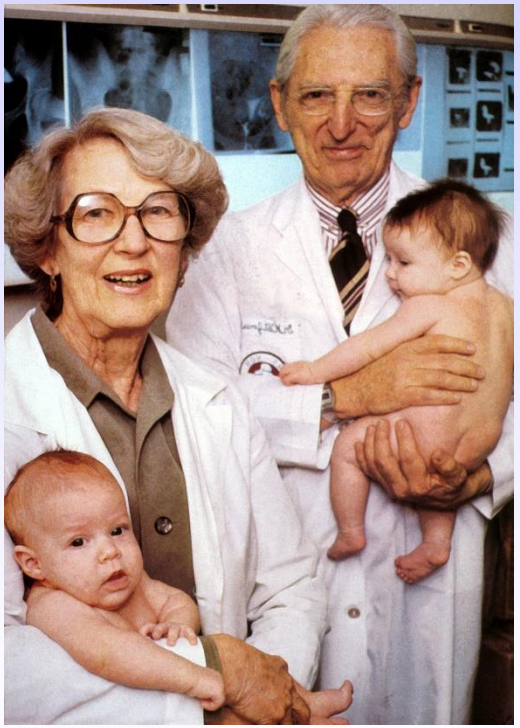
Memoir of a Medical Breakthrough



Foreword by
Elizabeth Jordan Carr Comeau

Howard and Georgeanna Jones

- Mandated retirement from Johns Hopkins in 1978
- Took positions at the Eastern Virginia Medical School in Norfolk, Virginia
- Moved to Norfolk the day Louise Brown born
- Based on television interview, previous patient used family foundation to donate $5,000 for microscope and incubator



The Team

1979 – 1980

- Howard and Georgeanna Jones
- Anibal Acosta
- Jairo Garcia
- Lucinda Veeck
- Two secretaries
- One office nurse
- Two O.R. nurses
- One clinical fellow/one computer wiz resident
- Four EVMS-ODU collaborators (Sandow, Wright, Witmyer, Wortham)

First Problems

- Certificate of Need
- Public hearing Oct. 31, 1979
- Extreme controversy
- General misunderstanding of the process

1/8/80

Test-tube baby lab OK'd; foes pledge court battle

By SANDY BAKSYS and JULIA WALLACE
Ledger-Star Staff Writers

NORFOLK — State Health Commissioner James Kenley today approved plans for an in vitro fertilization lab at Norfolk General Hospital, clearing the way for the first test-tube baby clinic in the United States.

Kenley, in a phone call to Norfolk General Hospital officials this morning, said the clinic violates no state or federal law.

Officials at the hospital and at Eastern Virginia Medical School, which is sponsoring the program, expressed delight with the decision. Doctors say they hope to try for the first pregnancy in March.

However, the president of the Tidewater Chapter of the Virginia Society for the initial stages of the program.

"We have great confidence that we will win the court battle if it goes that far," he said. The hospital, however, said it has not determined how far it will go in the courts.

Charles Dean, president of the Tidewater Chapter of the Virginia Society for Human Life, said he will appeal the decision.

"We'll never give up. That's exactly how we feel," Dean said.

"There's a lot of pressure against it. And a lot more is mounting. This isn't the end of it," Dean said.

He said the controversery was clouded by politics and no meaningful debates were held.

"The development and prestige of the Kenley would approve the clinic after so much public opinion against it.

He said the Virginia Society for Human Life will lead all court appeals. The funds for the appeals will come from individual donations, he added.

The lab, located next door to the obstetrics/gynecology unit at Norfolk General, is near completion. About $25,000 of hospital reserves were used to renovate and buy equipment.

During the in vitro process, a single egg will be removed from a woman within two hours of ovulation. The egg will then be fertilized with her husband's sperm in a glass dish. Any resulting embryo will be reimplanted in the woman's womb at the 8 or 16-cell stage, about two days after fertilization.

Monday, Feb. 11, 1980

Injunction Sought on Baby Lab

By SUSAN LOCKAMY
Virginian-Pilot Staff Writer

NORFOLK—Opponents of the nation's first "test-tube" baby project are asking state Atty. Gen. J. Marshall Coleman to help them block the opening of the project's laboratory at Norfolk General Hospital.

The Tidewater Chapter of the Virginia Society for Human Life, Inc., claims that State Health Commissioner James B. Kenley violated state requirements in granting on Jan. 8 the certificate-of-public-need for the lab.

In-Vitro Clinic Is Still Facing Firm Opposition

By MARIANNE ROBERSON
Staff Reporter

NORFOLK — Right-to-life groups' means possible to have the clinic closed.

Some of their efforts, such as a public statement that the Norfolk clinic

Living With the LH Surge

- Midnight, 1:30 am, 4:00 am cases
- Small team gathered with scientific enthusiasm
- Often too late and patient had ovulated
- On call around-the-clock
- Snowstorms (36 inches), floods, and hurricanes

1980

41	Patients monitored
19	Oocytes from natural cycles
13	Transfers
0	Pregnancies

Decision made by Dr. Georgeanna Jones to attempt mild ovarian stimulation in 1981 despite lack of success with these methods in the U.K.

How to stimulate normally-ovulating patients?

How to time hCG administration?

1981

13 attempts, some without oocytes, some without fertilization . .

World's First IVF Conference is held at Bourn Hall in 1981

The World's leading pioneers in IVF meet at Bourn Hall in September 1981.

Steptoe, Purdy and Edwards are seated on the right

Cloudy, in 30s tonight; rain chance Tuesday
Weather details on page A4
Monday, December 28, 1981

THE LEDGER-STAR

Final edition

Norfolk, Portsmouth, Virginia Beach, Chesapeake, Suffolk, Va.

106th year, no. 124 — 25 cents

Test-tube baby born in Norfolk is first in U.S.

By TERRY CARTER
and AMY GOLDSTEIN
Ledger-Star Staff Writers

NORFOLK — America's first "test-tube" baby, conceived here last spring and transplanted into the mother's uterus, was born this morning at Norfolk General Hospital.

It's a 5-pound, 12-ounce girl, named Elizabeth Jordan Carr.

The Eastern Virginia Medical School, which began attempts at in vitro fertilization in February 1980, announced that the baby was born at 7:56 a.m. The girl and her parents were reported doing fine, according to EVMS spokeswoman Vern Jones.

The mother is Judith Carr, a 28-year-old schoolteacher from Westminster, Mass. The father, Roger Carr, is a 30-year-old mechanical engineer.

The baby was delivered by Cesarean section by Dr. Mazen C. Andrews, chairman of the Department of Obstetrics and Gynecology at EVMS.

"The baby ... is in good condition," Andrews said. "This is just a symbol of the process, and I think a very happy one."

He said there were nine people in the delivery team "and each was indispensable in the technique." He singled out for special praise Drs. Howard and Georgeanna Jones, the husband-wife team that has spearheaded the in vitro effort.

"She's being treated as a normal newborn," said Dr. Fred Wirth, chief pediatrician at Norfolk General. He said doctors do not anticipate the baby's developing any special problems.

"She took an ounce of formula very well," he said. "She's already had her first feeding."

Andrews explained that the baby's mother checked into the hospital at 3 p.m. Sunday, officials said. She was still sleeping at each morning after giving birth.

Officials said Mrs. Carr was accepted into the program last Jan. 31, and a mature egg from her ovary was fertilized with her husband's sperm on April 15. Two days later, officials said, the embryo had grown to four cells and was transferred into Mrs. Carr's uterus.

Before entering the in vitro program, officials said, Mrs. Carr had three tubal pregnancies, and was referred to EVMS by her gynecologist.

> *'This is just a symbol of the process, and I think a very happy one.'*
> — Dr. Mazen C. Andrews

Three other women have been fertilized at the EVMS in vitro clinic and have not yet given birth, Jones said. The clinic failed in attempts to impregnate 41 women in 1980 but was successful in four of 10 attempts this year.

Earlier this year, the clinic began extracting as many as three eggs at a time from the mother to increase chances of conception. Fertility drugs containing hormones are used to increase the number of eggs the women produces each month.

Mrs. Carr's tubes had been removed because of a recurring problem with tubal pregnancies.

A crew from the British ITV network filmed the birth and is producing a one-hour television documentary, including interviews with the parents and the medical team, for the Boston affiliate of the Public Broadcasting Service.

The documentary's producer and reporter, Peter Williams, made a similar film three years ago on the birth of the world's first "test-tube" baby in England.

"Mazen Andrews had seen the film and liked it. That's why we're making the documentary," Williams said today.

The world's first "test tube" baby, also a 5-pound, 12-ounce girl, was born July 25, 1978 in Oldham, England. Their birth was the culmination of 12 years of experimentation and research by Dr. Patrick Steptoe, one of Britain's leading gynecologists, and Dr. Robert Edwards, a Cambridge University physiologist.

Last month, Steptoe said 20 in vitro babies had been born this year in England and Australia.

Karen Corrigan, spokeswoman for Norfolk General Hospital, said today that "We are all excited and ecstatic. Everybody is happy and excited and thrilled."

Earlier this month the Ladies' Home Journal carried an article about the first American woman to give birth to a test-tube baby. The woman, who lives on the West Coast but was not identified at her request, had been treated at the Steptoe-Edwards clinic in England.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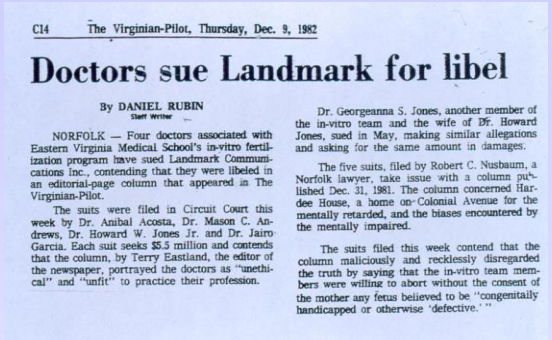
SAVING AFR
BIG ANIMAL
A radical plan to
butcher some
and sell their
November 1982/$2.00
TEST-TUBE BABY BOOM
Elizabeth Carr, America's first in vitro baby, at the lab where she was conceived

Dr. Georgeanna Takes On The Norfolk Press



C14 The Virginian-Pilot, Thursday, Dec. 9, 1982

Doctors sue Landmark for libel

By DANIEL RUBIN
Staff Writer

NORFOLK — Four doctors associated with Eastern Virginia Medical School's in-vitro fertilization program have sued Landmark Communications Inc., contending that they were libeled in an editorial-page column that appeared in The Virginian-Pilot.

The suits were filed in Circuit Court this week by Dr. Anibal Acosta, Dr. Mason C. Andrews, Dr. Howard W. Jones Jr. and Dr. Jairo Garcia. Each suit seeks $5.5 million and contends that the column, by Terry Eastland, the editor of the newspaper, portrayed the doctors as "unethical" and "unfit" to practice their profession.

Dr. Georgeanna S. Jones, another member of the in-vitro team and the wife of Dr. Howard Jones, sued in May, making similar allegations and asking for the same amount in damages.

The five suits, filed by Robert C. Nusbaum, a Norfolk lawyer, take issue with a column published Dec. 31, 1981. The column concerned Hardee House, a home on Colonial Avenue for the mentally retarded, and the biases encountered by the mentally impaired.

The suits filed this week contend that the column maliciously and recklessly disregarded the truth by saying that the in-vitro team members were willing to abort without the consent of the mother any fetus believed to be "congenitally handicapped or otherwise 'defective.' "

- Newspaper article published in the Virginian Pilot five days after Elizabeth's birth stating that abortions were mandated without parental consent by our clinical staff for patients carrying abnormal IVF fetuses
- GSJ sues for libel and wins a settlement; this money was donated for developing research projects

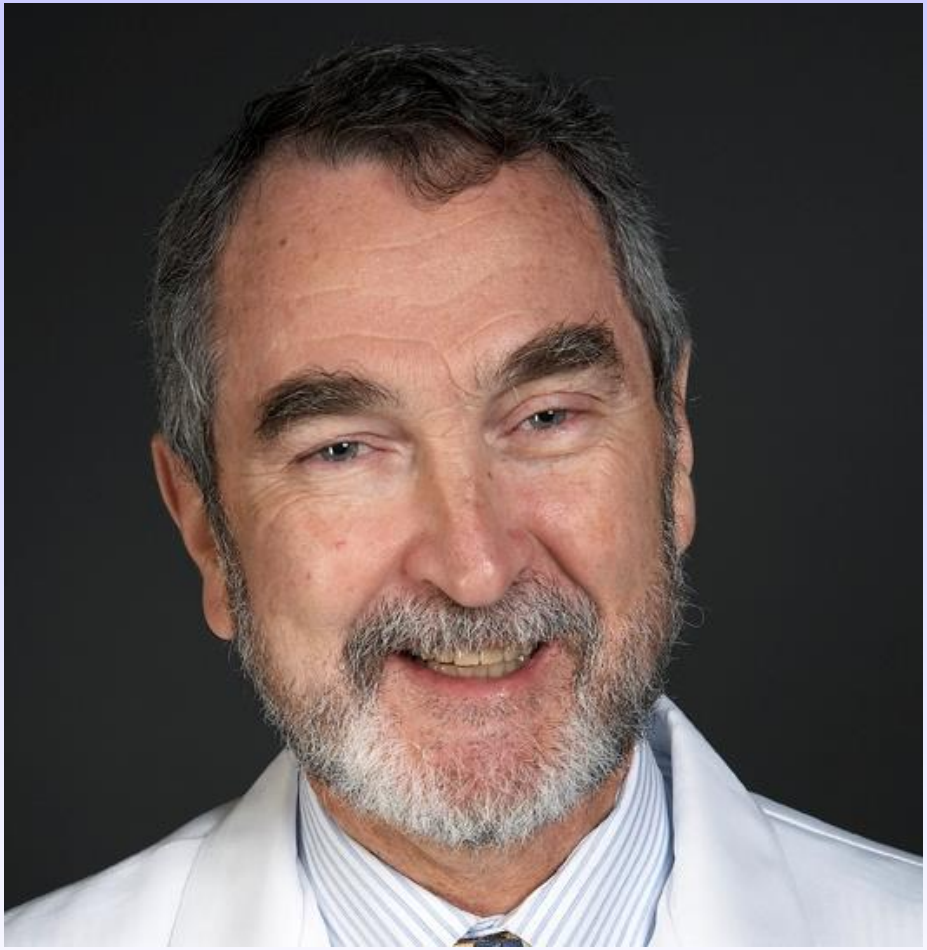
Some Pioneers and Pioneering Events in the IVF Laboratory

1. Embryo Culture
2. Cryobiology
3. Micromanipulation for andrology
4. Reproductive Genetics

Somatic Cell Media Used for Human IVF and Embryo Culture

Year	*Investigator*	*Medium*	*Use*
1880	Ringer	salt soln	amphib. heart
1907	Tyrode	salt soln	intestine
1943	Earle	salt soln	somatic
1950	Morgan et al.	Med 199	somatic
1956	Eagle	MEM	somatic
1963	Ham	F-10	somatic

Prof. Yves Menezo
B-1, B-2 Media



Dr. Patrick Quinn
HTF, Quinn’s series media

Prof. Henry Leese

Students:

David Gardner
Daniel Brison
Joe Conaghan
Karen Martin
Nicki Boland
Laura Hewitson
Franchesca Houghton
Roger Sturmey

Visiting Scientists:

Jeremy Thompson
Steve Downs

The 'new generation' media

The special importance of Amino Acids

Bavister (hamster)
Rieger (bovine)
Gardner and Lane (mouse/sheep): formulation of *'SOFaa'*
Hardy and Devreker (human)
Glutamine: Ammonium

Menezo: biochemical studies on amino acids and role of BSA/serum as a source of amino acids (B2 medium)

Forerunner of work which related amino acid profiling to developmental outcome: human/bovine (Houghton, Brison, Sturmey) oocyte (Picton)

Pivotal work on glucose (Gardner and Lane)

In addition to growing more blastocysts – **search for methods of embryo selection**

slide courtesy of Henry Leese

Prof. David K. Gardner
SOFaa, G-series media

Gardner → Lane → Zander-Fox → McPherson

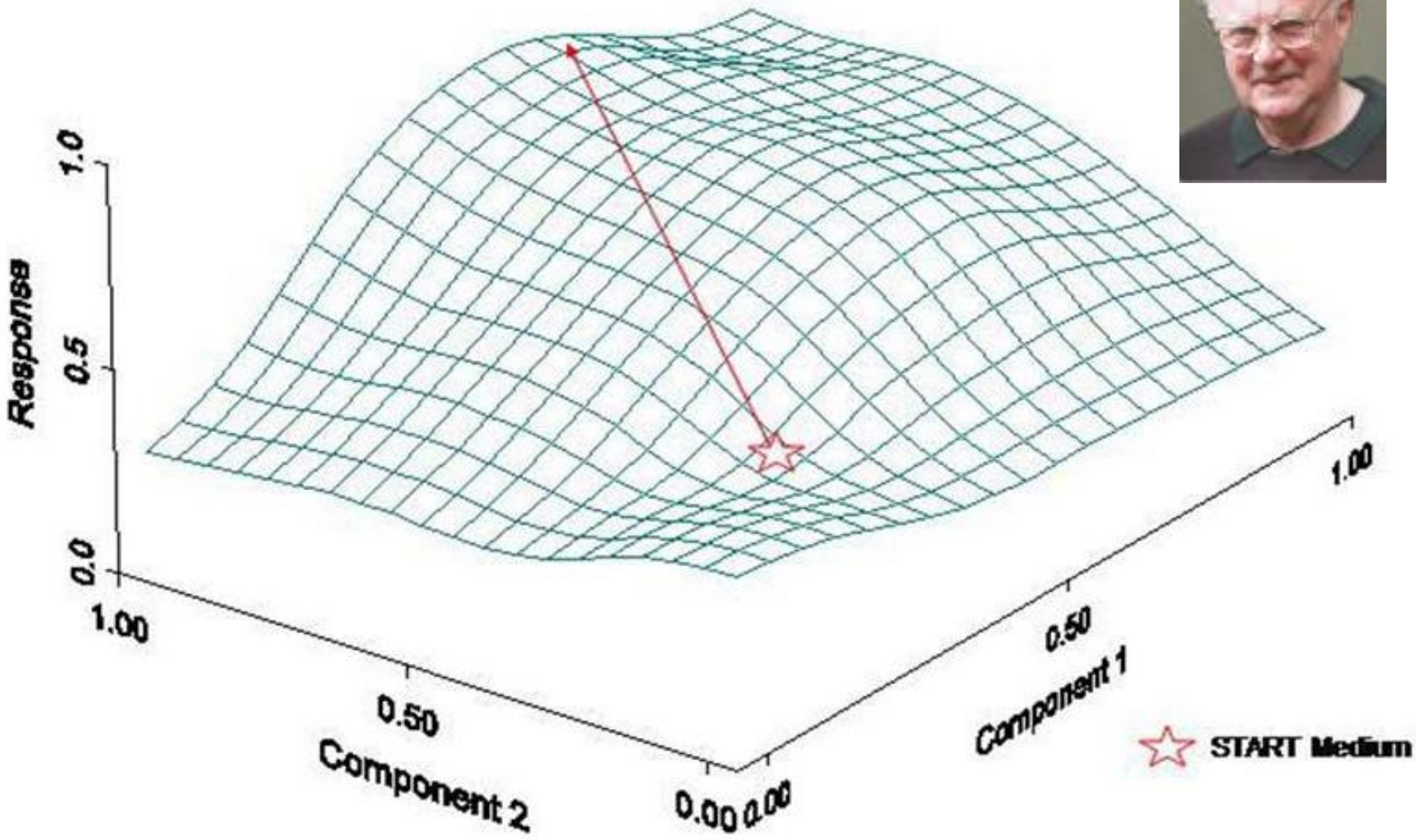
Let the embryo choose : *Empirical optimisation*

Simplex optimisation

- **John Biggers, Joel Lawitts** (1991)
- Use of engineering-based strategy to optimise constituents for mouse embryo culture (especially, overcoming the '2-cell block'
- Requires very high numbers of embryos for testing
- Resulted in KSOM and KSOM aa: excellent, if unphysiological media for growing mouse embryos
- Impossible to optimise every component
- 'No guarantee that the maximum response is the natural response' (**Summers and Biggers 2003**)
- Inappropriate strategy for optimising human embryo culture media – **but,** an outstanding achievement!

slide courtesy of Henry Leese

Three-dimensional concentration response-surface



(from Prof. John Biggers)

Dr. Stanley P. Leibo

Dr. Masa Kuwayama

Dr. Peter Mazur

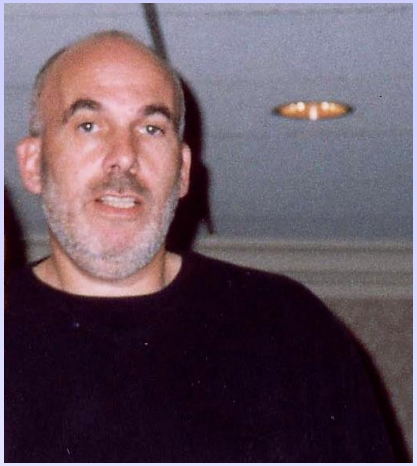
Dr. Greg Fahy and Dr. Bill Rall

B. Lassalle, J. Testart, J.P. Renard

Dr. Jacques Cohen

Dr. James Stachecki

Micromanipulation for Male Factor



Dr. Jacques Cohen, RBA lab
PZD

Dr. Michael Tucker, RBA
UZI, SUZI

Micromanipulation for Male Factor

Dr. Gianpero Palermo
ICSI

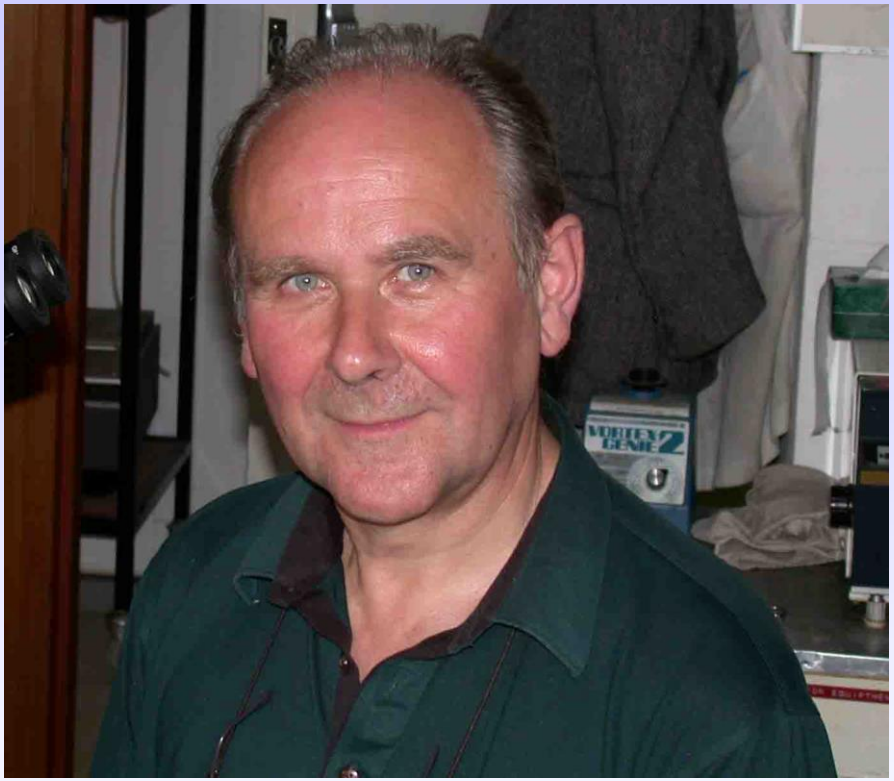
Dr. Michael Tucker
DSI

Preimplantation Genetic Diagnosis

Dr. Alan Handyside

Dr. Marcus Hughes

Preimplantation Genetic Diagnosis



Sir Richard Gardner

trophectoderm biopsy

Certification for US Embryologists

Dr. Brooks Keel

Dr. Richard Rawlins

Thank you.