

ovum transport and fertility regulation



WHO symposium
san antonio, texas 1975

ovum transport and fertility regulation



WHO symposium
san antonio, texas 1975

Ovum Transport and Fertility Regulation

Proceedings of a Meeting of the
Task Force on Methods for the Regulation of Ovum Transport
organized by
the World Health Organization
and held at the Lutcher Conference Center of the
University of Texas, San Antonio
on 23–27 June 1975



EDITED BY

M. J. K. Harper
WHO, Geneva, Switzerland

C. J. Pauerstein
San Antonio, USA

C. E. Adams
Cambridge, UK

E. M. Coutinho
Bahia, Brazil

H. B. Croxatto
Santiago, Chile

D. M. Paton
Edmonton, Canada

PUBLISHED BY

Scriptor
Copenhagen
1976

Authors alone are responsible for the views
expressed in the Proceedings.

The mention of specific companies or of
certain manufacturers' products does not imply
that they are endorsed or recommended by the
World Health Organization
in preference to others of a similar nature
that are not mentioned.

A limited number of copies of this publication
are available for distribution from
The Human Reproduction Unit,
World Health Organization,
1211 Geneva 27, Switzerland.

Printed in Denmark
by Bogtrykkeriet Forum
Copenhagen

ISBN 87-87473-07-0

Contents

List of participants	11
The quest for a contraceptive method for the regulation of Ovum Transport	
<i>M. J. K. Harper and C. J. Pauerstein</i>	15

SECTION I	Biophysical and Bioengineering Considerations in Studies of Oviductal Physiology	
	Moderator: <i>R. J. Blandau</i>	
	A biophysical model of the mechanisms regulating ovum trans- port rates	
	<i>M. L. Chatkoff</i>	27
	A system for measurement of oviductal motility and contractility and chronic changes in luminal diameter	
	<i>W. D. Blair and L. R. Beck</i>	41
	Microminiature transducers for oviductal motor function	
	<i>T. S. Nelsen, T. A. Nunn, and J. B. Angell</i>	75
	Methods for studying ovum transport rates	
	<i>R. J. Crosby, M. L. Chatkoff, and C. J. Pauerstein</i>	99
	Physiologic assessment of oviductal motility – extraluminal tele- metric subject evaluation	
	<i>E. Fromm, C-R. Garcia, and D. C. Jeutter</i>	107
	Stochastic elements in the development of deterministic models of egg transport	
	<i>P. Verdugo, R. J. Blandau, P. Y. Tam, and S. A. Halbert</i>	126
	DISCUSSION PAPER:	
	An overview of gamete transport – comparative aspects	
	<i>R. J. Blandau and P. Verdugo</i>	138
	SUMMARY OF DISCUSSIONS on Biophysical and Bioengineering Con- siderations In Studies of Oviductal Physiology	
	Reporter: <i>C. J. Pauerstein</i>	147

SECTION II	Oviductal Contractility	
	Moderators: <i>J. M. Marshall</i> and <i>E. E. Daniel</i>	
	Studies of oviductal contractility (overview of <i>in vitro</i> approach)	
	<i>J. M. Marshall</i>	153
	Electrophysiology of the oviduct	
	<i>A. Talo</i>	161
	Relationship between cyclic AMP levels and oviductal contractility	
	<i>H. Maia, Jr., I. Barbosa, and E. M. Coutinho</i>	168
	The role of calcium in contraction of the oviduct	
	<i>B. J. Hodgson and S. Daly</i>	182
	Prostaglandins, oviductal motility and egg transport	
	<i>C. H. Spilman</i>	197
	Acquisition and computer analysis of oviductal motility data	
	<i>C. H. Spilman and M. L. Sutter</i>	212
	Motility of the human oviduct <i>in vivo</i>	
	<i>H. Maia and E. M. Coutinho</i>	221
	DISCUSSION PAPER:	
	A critical introduction to analysis of the role of oviductal motility in ovum transport	
	<i>E. E. Daniel</i>	228
	SUMMARY OF DISCUSSIONS on Oviductal Contractility	
	Reporter: <i>E. M. Coutinho</i>	237

SECTION III	Autonomic Mechanisms in Ovum Transport	
	Moderators: <i>D. L. Black</i> and <i>J. Brundin</i>	
	Adrenergic mechanisms in ovum transport	
	<i>J. Brundin</i>	243
	Autonomic nerves and related amine receptors mediating motor activity in the oviduct of monkey and man. A histochemical, chemical, and pharmacological study	
	<i>Ch. Owman, B. Falck, E. D. B. Johansson, E. Rosengren, N-O. Sjöberg, B. Sporrang, K-G. Svensson, and B. Walles</i>	256

Correlation of plasma estrogens and progesterone levels with the <i>in vitro</i> adrenergic responses in the isthmus of the human oviduct <i>A. H. Moawad, P. Hedqvist, and M. H. Kim</i>	276
Adrenergic mechanisms in rabbit and human oviducts <i>D. M. Paton</i>	293
Adrenergic mechanisms and hormonal status of the oviduct <i>H. Takeda and M. Doteuchi</i>	307
Effects of prostaglandins on oviductal contractility and egg transport in rabbits <i>I. Aref and E. S. E. Hafez</i>	320
Effects of adrenergic drugs or denervation on ovum transport in rabbits <i>J. P. Polidoro, R. D. Heilman, R. M. Culver, and R. R. Reo</i> ..	331
Cholinergic mechanisms, oviductal motility and ovum transport <i>G. R. Howe</i>	342
DISCUSSION PAPER:	
Autonomic mechanisms in ovum transport – summary and conclusion <i>D. L. Black</i>	350
SUMMARY OF DISCUSSIONS ON Autonomic Mechanisms in Ovum Transport	
Reporter: <i>D. M. Paton</i>	354

SECTION IV

Control of Ovum Transport in the Oviduct

Moderators: *J. P. Bennett* and *E. S. E. Hafez*

Anatomical and physiological mechanisms of ovum transport <i>E. S. E. Hafez</i>	361
Retention of unfertilized ova in the oviducts of mares <i>C. H. Van Niekerk</i>	375
Possible role of the embryo in the control of oviductal transport in mares <i>K. J. Betteridge, P. F. Flood, and D. Mitchell</i>	381
Ovum transport in non-human primates <i>G. A. Eddy, R. G. Garcia, D. C. Kraemer, and C. J. Pauerstein</i>	390

Transport of ovum surrogates by the human oviduct	
<i>J. Díaz, J. Vázquez, S. Díaz, F. Díaz, and H. B. Croxatto</i>	404
Ovum transport in women	
<i>S. Cheviakoff, S. Díaz, M. Carril, N. Patrilli, H. D. Croxatto, C. Lladós, M. E. Ortiz, and H. B. Croxatto</i>	416
Egg survival relative to maternal endocrine status	
<i>C. E. Adams</i>	425
DISCUSSION PAPER:	
Drug regulation of egg transport	
<i>J. P. Bennett</i>	441
SUMMARY OF DISCUSSIONS on Control of Ovum Transport in the Oviduct	
Reporter: <i>C. E. Adams</i>	466

SECTION V	Effects of Estrogen and Progesterone on Contractility and Ovum Transport	
	Moderators: <i>M. C. Chang</i> and <i>G. S. Greenwald</i>	
	Estrogen, progesterone and egg transport – overview and identification of problems	
	<i>M. C. Chang</i>	473
	<i>In vivo</i> human oviductal motility: effects of estrogen and progesterone	
	<i>E. Guiloff-Fische, A. Ibarra-Polo, and C. Gómez-Rogers</i>	485
	Influence of estrogen and progesterone on oviductal function	
	<i>K. W. Humphrey</i>	495
	Estrogen, progesterone, oviductal function and ovum transport	
	<i>J. N. Karkun</i>	506
	Influence of timing and dose of progesterone on ovum transport rates	
	<i>M. I. G. de Vargas and C. J. Pauerstein</i>	515
	Progesterone binding protein in cytosol fraction from human oviduct	
	<i>B. E. Fuentealba, G. Escudero, and G. E. Swaneck</i>	527

DISCUSSION PAPER:

Effects of estrogen and progesterone on egg transport:

Summary and conclusions

G. S. Greenwald 539

EPILOGUE:

Interference with ovum transport: Implications for fertility control

E. M. Coutinho 544

SUMMARY OF DISCUSSIONS on Effects of Estrogen and Progesterone on Contractility and Ovum Transport

Reporter: *H. B. Croxatto* 557

EPILOGUE

Implications for the Development of a Clinically Useful Contraceptive

M. J. K. Harper and C. J. Pauerstein 563

SYMPOSIUM ON OVUM TRANSPORT AND FERTILITY REGULATION

San Antonio, Texas, 23-27 June 1975

List of Participants

Dr. C. E. Adams

Agricultural Research Council
Unit of Reproductive Physiology
and Biochemistry
Cambridge, England

Dr. I. Aref

Department of Obstetrics & Gynecology
and Human Reproduction Research Unit
Al-Azhar University School of Medicine
Darrasa-Cairo, Egypt

Dr. J. P. Bennett

Syntex (US), Inc.
Palo Alto, California, USA

Dr. K. J. Betteridge

Physiology Section
Health of Animals Branch
Animal Diseases Research Institute
Ottawa, Ontario, Canada

Dr. G. Bialy

Contraceptive Development Branch
Center for Population Research
National Institute of Child Health
and Human Development
Bethesda, Maryland, USA

Dr. D. L. Black

Department of Animal Physiology
Laboratory for Reproductive Physiology
Paige Laboratory
Amherst, Massachusetts, USA

Dr. W. D. Blair

Department of Obstetrics & Gynecology
The University of Alabama in Birmingham
Birmingham, Alabama, USA

Dr. R. J. Blandau

Department of Biological Structure
University of Washington
School of Medicine
Seattle, Washington, USA

Dr. J. Brundin

Department of Obstetrics & Gynecology
Karolinska Institute
Danderyds Hospital
Danderyd, Sweden

Dr. M. C. Chang

The Worcester Foundation
for Experimental Biology
Shrewsbury, Massachusetts, USA

Dr. M. L. Chatkoff

Department of Obstetrics & Gynecology
and Biochemistry
Center for Research and Training in
Reproductive Biology
The University of Texas Health
Science Center
San Antonio, Texas, USA

Dr. S. Cheviakoff

Centro de Estudios en Biología
de la Reproducción
Universidad de Chile
Santiago, Chile

Dr. E. M. Coutinho

Department of Maternal Health
and Child Care
Maternidade Climerio de Oliveira
Universidade Federal da Bahia
Salvador, Bahia, Brazil

Mr. R. Crosby

Department of Obstetrics & Gynecology
Center for Research and Training in
Reproductive Biology
The University of Texas Health
Science Center
San Antonio, Texas, USA

Dr. H. B. Croxatto

Departamento de Fisiología y Embriología
Instituto de Ciencias Biológicas
Universidad Católica de Chile
Santiago, Chile

Dr. E. E. Daniel

Department of Pharmacology
The University of Alberta
Edmonton, Alberta, Canada

Dr. J. Díaz

Departamento de Fisiología y Embriología
Instituto de Ciencias Biológicas
Universidad Católica de Chile
Santiago, Chile

Dr. M. Doteuchi

Shionogi Research Laboratory
Shionogi & Company, Ltd.
Osaka, Japan

Dr. C. A. Eddy

Department of Obstetrics & Gynecology
and Physiology
Center for Research and Training in
Reproductive Biology
The University of Texas Health
Science Center
San Antonio, Texas, USA

Dr. E. Fromm

Department of Biological Sciences
Drexel University
Philadelphia, Pennsylvania, USA

Dr. B. Fuentealba

Departamento de Fisiología y Embriología
Instituto de Ciencias Biológicas
Universidad Católica de Chile
Santiago, Chile

Dr. G. S. Greenwald

Department of Obstetrics & Gynecology
and Anatomy
University of Kansas Medical Center
Kansas City, Kansas, USA

Dr. E. Guiloff

Department of Obstetrics & Gynecology
Jose-Joaquin Aguirre Hospital
University of Chile
Santiago, Chile

Dr. E. S. E. Hafez

Department of Gynecology-Obstetrics
and Physiology
Wayne State University
School of Medicine
Detroit, Michigan, USA

Dr. B. J. Hodgson

Department of Obstetrics & Gynecology
and Pharmacology
Center for Research and Training in
Reproductive Biology
The University of Texas Health
Science Center
San Antonio, Texas, USA

Dr. G. R. Howe

Laboratory for Reproductive Physiology
Paige Laboratory
University of Massachusetts
Amherst, Massachusetts, USA

Dr. K. Humphrey

18 Lennox Street
Gordon, Sydney, Australia

Dr. A. Ibarra-Polo

Department of Obstetrics & Gynecology
Jose-Joaquin Aguirre Hospital
University of Chile
Santiago, Chile

Dr. J. N. Karkun

Division of Endocrinology
Central Drug Research Institute
Lucknow, India

Dr. D. Kennedy

Department of Medical Science
Neurosciences Section
Brown University
Providence, Rhode Island, USA

Dr. H. Koester

Department of Obstetrics & Gynecology
Staedtische Frauenklinik
Dortmund, Federal Republic of Germany

Dr. D. Kraemer

Department of Veterinary Physiology
and Pharmacology
Texas A & M University
College of Veterinary Medicine
College Station, Texas, USA

Dr. H. Maia

Department of Obstetrics & Gynecology
Maternidade Climerio de Oliveira
Universidade Federal da Bahia
Salvador, Bahia, Brazil

Dr. H. Maia, Jr.

Department of Obstetrics & Gynecology
Maternidade Climerio de Oliveira
Universidade Federal da Bahia
Salvador, Bahia, Brazil

Dr. J. M. Marshall

Department of Medical Science
Neurosciences Section
Brown University
Providence, Rhode Island, USA

Dr. A. H. Moawad

Department of Physiology
Karolinska Institutet
Stockholm, Sweden

Dr. T. S. Nelsen

Department of Surgery
Stanford University School of Medicine
Stanford, California, USA

Dr. C. Owman

Department of Histology
University of Lund
Lund, Sweden

Dr. D. M. Paton

Department of Pharmacology
University of Alberta
Edmonton, Alberta, Canada

Dr. C. J. Pauerstein

Department of Obstetrics & Gynecology
and Physiology
Center for Research and Training in
Reproductive Biology
The University of Texas Health
Science Center
San Antonio, Texas, USA

Dr. J. P. Polidoro

Division of Pharmacology
Ortho Research Foundation
Raritan, New Jersey, USA

Dr. C. H. Spilman

Fertility Research
The Upjohn Company
Kalamazoo, Michigan, USA

Dr. A. Talo

Department of Zoology
University of Turku
Turku, Finland

Dr. C. H. Van Nierkerk

Department of Human and
Animal Physiology
University of Stellenbosch
Stellenbosch, South Africa

Dr. M. I. Vargas

Department of Obstetrics & Gynecology
Center for Research and Training in
Reproductive Biology
The University of Texas Health
Science Center
San Antonio, Texas, USA

Dr. P. Verdugo

Department of Bioengineering
University of Washington
School of Medicine
Seattle, Washington, USA

WHO SECRETARIAT**Dr. M. J. K. Harper**

Human Reproduction Unit
World Health Organization
Geneva, Switzerland

THE QUEST FOR A CONTRACEPTIVE METHOD FOR THE REGULATION OF OVUM TRANSPORT

In 1972, the World Health Organization launched a major research programme directed toward development of safe, acceptable, and effective methods for the regulation of human fertility.

Although presently available methods are considerably advanced over past methods, they remain relatively crude, and fail to meet the varied requirements of consumers and services in different countries, particularly developing ones. For these reasons, what has become known as the WHO Expanded Programme of Research, Development, and Research Training in Human Reproduction aims at improvement of existing methods of fertility regulation, assessment of their suitability in different populations, and development of new technology.

A major portion of the research effort is conducted by multidisciplinary, multinational collaborative Task Forces working in priority areas identified by the Advisory Group to the Expanded Programme. Initially, a review of the state of knowledge current in the particular field is made, and various approaches to the development of new methods of fertility control are discussed: a strategic plan is then developed that includes definition of short-term, intermediate, and long-term objectives. The steps by which the objectives can be achieved and initial estimates of the time and costs involved are identified. After approval by WHO, scientists who can make contributions to the research are invited to participate. All research projects are assessed on technical and ethical grounds by the Task Force and by an independent Review Group; those that are approved are supported by WHO.

The Advisory Group made the following statement at a meeting in January, 1972:

"It has been repeatedly shown, mainly in animal studies, that post-ovulatory fertility control can be achieved by interference with ovum transport in the Fallopian tube, and by altering implantation mechanisms in the uterus by

non-steroidal and steroidal compounds. Accordingly a Task Force which included research on the reproductive processes involved, on pharmacological models, on contraceptive screening, and on clinical work where feasible in this area, could accelerate the development of post-ovulatory anti-fertility agents for human use. More specifically, such a Task Force would concern itself with components such as: (a) tubal events, e. g. ovum transport and development, and the hormonal, metabolic and pharmacodynamic milieu in which these events occur; (b) the uterine events, particularly around the time following implantation; e. g. development and differentiation of the blastocyst and the hormonal, metabolic (enzymatic, osmotic and ionic) and haemodynamic changes in the endometrium related to the implantation of the blastocyst; (c) compound synthesis based on research on tubal and uterine events and systematic "structure" activity relationship studies, for animal screening of potential post-ovulatory fertility regulating agents; and (d) clinical pharmacological studies where possible."

As a result the first meeting of a Task Force on Methods to Regulate Ovum Transport and Implantation was held in March, 1972, in Geneva. At this meeting, 11 scientists from 7 countries, and 4 members of WHO secretariat met to prepare a plan of action for the Task Force.

The group emphasized goal-oriented clinical problems, and recognized that chances of obtaining applicable results from existing animal models were remote. However, pertinent animal studies, especially in cases where human experimentation was not possible, were considered profitable.

Priority research areas were identified under three broad headings: (1) regulation of implantation, (2) regulation of events in the oviduct, and (3) intra-vaginal delivery systems for release of microdose progestins and other agents. This last area was considered a priority area by the participants in this meeting, although it was recognized that the mode of action of such a system could be not only on ovum transport and implantation, but also on sperm transport in the female reproductive tract.

With specific respect to the regulation of events in the oviduct, the following recommendations were made:

"The objective of this Task Force group is to develop a variety of fertility regulating agents and methods which interfere with fertilization and/or transport of the fertilized ovum.

Fertility regulation may be achieved by interference with the transport and metabolism of the fertilized ovum in the oviduct. However, there is insufficient knowledge concerning the factors that control normal oviductal motility and ovum transport. It is proposed to obtain information on such factors in untreated women and in women using various drugs for post-coital contraception. It is also proposed to recover the fertilized human ovum from the uterine cavity and to estimate the time required for this transport under normal cir-