

# ANTIFERTILITY COMPOUNDS IN THE MALE AND FEMALE

*Development, Actions and Applications of Chemicals Affecting the Reproductive Processes of Animals, Insects and Man*

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The first book in monograph form to cover chemical agents affecting the fertility of both mammalian sexes at experimental levels . . . developments in the exciting field of insect chemosterilants and the complementary pheromones (insect attractant chemicals).

Provides also a condensed account of present uses of steroidal chemicals in human fertility control. The subject is brought within the range of less informed readers by the inclusion of appropriate background information -- particularly concerning physiological mechanisms involved in the control of reproductive processes.

*American Lecture Series®*



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**ANTIFERTILITY COMPOUNDS IN  
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AMERICAN LECTURE SERIES®

*A Monograph in*  
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*Edited by*  
I. NEWTON KUGELMASS, M.D., Ph.D., Sc.D.  
*Consultant to the Departments of Health and Hospitals*  
*New York, New York*

## FOREWORD

**O**UR LIVING CHEMISTRY SERIES was conceived by Editor and Publisher to advance the newer knowledge of chemical medicine in the cause of clinical practice. The interdependence of chemistry and medicine is so great that physicians are turning to chemistry, and chemists to medicine in order to understand the underlying basis of life processes in health and disease. Once chemical truths, proofs and convictions become sound foundations for clinical phenomena, key hybrid investigators clarify the bewildering panorama of biochemical progress for application in everyday practice, stimulation of experimental research, and extension of postgraduate instruction. Each of our monographs thus unravels the chemical mechanisms and clinical management of many diseases that have remained relatively static in the minds of medical men for three thousand years. Our new Series is charged with the *nisus élan* of chemical wisdom, supreme in choice of international authors, optimal in standards of chemical scholarship, provocative in imagination for experimental research, comprehensive in discussions of scientific medicine, and authoritative in chemical perspective of human disorders.

Dr. Jackson of Manchester gathers into fruitful comprehension the principles and practice of inducing artificial antifertility in the male and female with balanced alternation of guiding hypotheses and experimental tests. It gives us the current panorama of contraception in the light of the mechanism of reproduction. It provides the means for curbing the fundamental tendency in the materials of Nature to grow from more to more—atoms building up molecules, molecules uniting in micellae, these forming higher units or whole systems, all veering to produce life. We can sense where this newer knowledge of applied biology is

going, what kind of world it will produce, how it will affect present and future mankind. Biological or systemic control of conception involves prevention of gamete formation or release in male or female by inhibition of spermatogenesis or ovulation; prevention of fertilization; and/or prevention of implantation by inactivation of the fertilized egg or inhibition of progestational changes in the uterus. The male is thus viewed in terms of inhibition of spermatogenesis, hormonal control of fertility and chemotherapy with alkylating agents; and the female, in terms of ovogenesis and ovulation, ovarian function, steroid control of fertility and interference with gestation.

Two-thirds of the human race inhabit regions of uncontrolled fertility where the annual birth rate is about fifty per 1,000 population. The remaining one-third of the world's people inhabit areas of controlled fertility where the annual birth rate is about twenty-five per 1,000 population. The unprecedented rate of increase is accelerating not as a result of increased fertility but of decreased mortality. It took the world population to reach one billion from the beginning of time to 1850; two billion to 1930; three billion to 1960; and three billion more anticipated by 1990 in the absence of famine, pestilence and/or war. The ghost of Malthus is upon us with the current trend for the human population to increase geometrically. Such a rate of growth from the beginning of the Christian Era would have yielded a world of people numbering ninety billion times ten to the twelfth power. The problem of problems is how to deal with an overpopulation that faces us on all sides in an ever-shrinking interdependent world.

The problems of fertility control are always the same but the solutions differ with each society by virtue of physiologic, environmental, cultural and religious differences. Chemical and clinical research in antifertility methods and materials calls for acceptable means based on diverse action mechanisms. Animal experiments focused upon different links in the biologic chain of events in reproduction not only involve immunologic approaches with the formation of antibodies against gonad-stimulating hormones and against spermatozoa, but chemotherapy with anti-zygote and abortifacient activity respectively. One approach

will be superseded by another until scientific techniques are gradually improved to satisfy the demographic needs of all world societies and thus displace archaic ways of fertility control. Naturam mutare difficile est. Naturae sequitur semina quiesque suae.

*"Of the cell, the wondrous seed  
Becoming plant and animal and mind  
Unerringly forever after its kind,  
In its omnipotence, in flower and weed  
And beast and bird and fish, and many a breed  
Of man and woman, for all years behind  
Building its future."*

I. NEWTON KUGELMASS, M.D., PH.D., SC.D., *Editor*



## PREFACE

**W**ITH THE PREPARATION of this work the author has both the privilege and responsibility of producing for the first time, a monograph surveying the broad field of antifertility chemicals. This situation presents both advantages and disadvantages.

The present rate of publication of research papers is such that no sharp line has been drawn with regard to references of immediate interest. An attempt has been made to bring the subject within the range of less informed readers and to this end, appropriate background information has been included, particularly concerning physiological processes under discussion. For the same reason, generalisations and over-simplification have had to be made. The book lays no claim to being a popular manual on this subject, however. The text covers chemical agents affecting the fertility of both sexes in experimental animals, developments in the exciting field of insect chemo-sterilants and the complementary pheromones (insect attractant chemicals). It also provides a necessarily condensed account of the development and use of steroidal chemicals in human fertility control.

It is hoped that the general coverage will interest and stimulate research workers in this field and also appeal to many who are anxious to keep abreast with scientific progress in this complex and fascinating subject. As yet, it has barely gained a deserved entry into pharmacological text books or University teaching. Perhaps this presentation will serve to promote a positive drive forward in this direction.

## INTRODUCTION

**T**HE POTENTIAL GRAVITY of the human population problem is increasingly manifest in various world foci, and according to authoritative opinion, an extension in a matter of decades to disastrous levels is inevitable if present trends continue. It has even been suggested that no form of drug treatment may be available in time to provide effective control on an adequate scale.

The object of this monograph is to provide a general picture of the present situation and prospects, regarding the development of specific chemicals suppressing fertility when given by the oral route. Serious endeavour to control human reproduction in this way dates back only 15 years or so and much scientific research remains in its preliminary stages with experimental animals. Considering the natural prejudices to be overcome, the lack of highly organized basic research groups and financial support, surprising progress has been made towards the specific interference with different stages of the highly complex, mammalian reproductive processes.

The selection of antifertility chemicals for human use presents a unique pharmacological problem. It requires the elaboration of non-toxic, inexpensive compounds for administration to healthy adult reproductive age groups on a scale far beyond that of any drug so far used by medical science. Ideally, such compounds, by occasional administration, should produce and maintain sterility as desired, without interference with sexual activity or subsequent adverse effects upon reproductive capacity or progeny.

In the face of these stringent requirements, is the development of antifertility compounds for human use likely to succeed?

Reproductive tissues and processes exhibit a variety of unique features and mechanisms, implying the possibility of selective pharmacological interference without serious disturbance of the function of other body tissues.

It is, however, unlikely that effective compounds will be non-toxic and pressures of population growth may compel the acceptance of certain risks; unless of course, alternative approaches—mechanical devices or surgical sterilization—can be applied on an adequate scale. Important by-products of reproductive pharmacology include increase in fundamental knowledge of reproductive processes and their control, particularly concerning the dynamics and mechanisms of cell proliferation and differentiation. Important applications of ‘antifertility’ chemicals also lie in the fields of pest control and animal husbandry.

Many years of intensive research and clinical experience with steroidal sex hormones preceded the present successful utilization of various hormone derivatives as oral contraceptives in women. The method is inapplicable on a global scale and must be considered an interim procedure, ultimately to be superseded by simpler procedures. In the male, the problem is entirely different and formidable difficulties beset the transposition from laboratory animal to man. No compound for the male has reached the stage of contraceptive trials, although it may be said that the foundations have been laid for the eventual control of fertility in man. It must be stressed, however, that little is known of the results of prolonged suppression of fertility on reproductive capacity or the heritable consequences of chemical interference with the developing sex cells. The highest degree of security must be provided and a great deal of systematic research is required if worthwhile advances are to be made.

## ACKNOWLEDGMENTS

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H. J.

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