THE NEED FOR FAMILY PLANNING

Family planning is a socially beneficial activity that affects the well-being of women, men, children, families, and society as a whole. Planned fertility confers the benefits of improved child health and development and reduces the lifetime risk of chronic illness or death from a pregnancy-related condition.

A woman experiencing an unintended pregnancy is at greater risk for depression and physical abuse. She also faces the usual health risks of pregnancy, including maternal death. Closely spaced births carry additional health risks for the mother and child. The child born from an unplanned conception is at greater risk of low birth weight, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development. With an unplanned conception, the mother and father may suffer economic hardship and may fail to achieve their educational and career goals, and their relationship is at greater risk of dissolution.

According to a recent analysis by the Global Health Council, the world’s 1.3 billion women between the ages of 15 and 45 experienced more than 1.2 billion pregnancies in the 6 years between 1995 and 2000. Of these, more than 300 million or more than one-quarter were unintended, and nearly 700,000 women died as a result of unintended pregnancies. The number of women at risk for unplanned pregnancies will grow as the world’s population continues to rise. Over the next decade, 600 million girls are projected to reach adolescence, which will be the largest cohort of young women in human history.

Although a number of reversible and nonreversible contraceptive methods are generally effective (barrier methods, hormonal methods, intrauterine devices, and contraceptive sterilization), no method is 100 percent effective for all users, and some men and women experience undesirable side effects.
Most men and women spend the majority of their reproductive years trying to avoid conception, and their contraceptive preferences change during the 30 years that they typically need contraception. Methods are needed for child spacing as well as permanent pregnancy prevention; for young people and those approaching menopause; for postpartum and breast-feeding women; for women and men with medical conditions that restrict contraceptive options; for those with few resources; for those with limited access to medical care; and for those whose situations make correct and consistent use difficult. The cultural or personal unacceptability of the various methods also points to the need for new options. In addition, the development of new methods that protect against pregnancy as well as against Sexually Transmitted Infections (STIs) would be enormously beneficial, as the HIV/AIDS pandemic threatens world health and continues to devastate sub-Saharan Africa and Asia.

**NEW ADVANCES**

Recent scientific and technological advances in genomics, proteomics, new materials, new drug delivery systems, and a new understanding of reproductive biology offer the promise of new, safe, and effective forms of contraception. At the same time, new global consortia working in this area are beginning to provide improved structures to pursue these opportunities collaboratively. The development of novel contraceptives would help alleviate the growing unmet demand for satisfactory contraception and would improve the lives of families everywhere. Given the unprecedented opportunities for new progress in the field, now is the time to move forward with a bold research agenda.

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**Defining the Key Criteria for Novel Contraceptive Target Selection**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Examples of Desirable Characteristics</th>
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</thead>
<tbody>
<tr>
<td>Expression</td>
<td>Uniquely or selectively expressed in reproductive tract tissue or organs involved in reproduction</td>
</tr>
<tr>
<td>Function</td>
<td>Inhibiting function specifically and completely disrupts or alters a process unique to reproduction</td>
</tr>
<tr>
<td>Timing of action</td>
<td>Close to time of fertilization (e.g., postmeiotic events in gametogenesis)</td>
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<tr>
<td>Potential for reversible modulation by a drug</td>
<td>Druggable protein classes such as enzymes, membrane proteins, receptors, and ion channels and transport proteins</td>
</tr>
<tr>
<td>Potential route of administration</td>
<td>Amenable to simple delivery systems ensuring ease of use and high rates of compliance</td>
</tr>
<tr>
<td>Potential for product manufacture</td>
<td>Inexpensive and easy to produce</td>
</tr>
<tr>
<td>Potential for noncontraceptive benefits</td>
<td>Dual protection against sexually transmitted infections and conception; protection against cancer or other diseases</td>
</tr>
</tbody>
</table>
RESEARCH PRIORITIES

This report builds on Contraceptive Research and Development: Looking to the Future (Institute of Medicine, 1996), the most recent of several IOM reports about the future of contraceptive research and development. Many of the recommendations put forth in that report are as relevant today as they were in 1996, but the recent unprecedented advances in science and technology warrant a fresh examination of the research goals and agenda in the field of contraception. A major goal of the present committee was to identify ways in which new information and new technologies can be rapidly and efficiently applied to contraceptive target identification, validation, and product development.

The committee’s recommendations address (1) facilitation of the stages of contraceptive development from target selection to product development and clinical testing and (2) strategies for research success, including participation by developing countries, expansion of public-private partnerships, increased clinical and scientific training and career development in contraception, and strategic management of research efforts.

SUMMARY OF RECOMMENDATIONS: A BLUEPRINT FOR ACTION

Discovery: Identify and Validate Novel Contraceptive Targets (Chapter 2)
- Generate a complete reproductive transcriptome and proteome, and define genetic and protein networks
- Generate reproductive lipidomes and glycomes
- Validate existing and emerging contraceptive targets

Translation: Enhance Contraceptive Drug Discovery, Development, and Clinical Testing (Chapters 3 and 4)
- Develop high-throughput screening facilities
- Facilitate translational research
- Facilitate the development of appropriate drug delivery systems
- Develop new approaches to measure contraceptive efficacy
- Integrate behavioral research at an early stage of development
- Discover, enhance and promote potential health benefits of existing and new methods, and intensify efforts to develop new contraceptive methods that are prophylactic for HIV infection and other STIs

Implementation: Facilitate and Coordinate Future Implementation of Contraceptive Research and Development (Chapter 5)
- Expand public-private partnerships for contraceptive development
- Increase the participation of developing countries in contraceptive development
- Increase training and career development opportunities in contraception
- Establish an ongoing Forum on Contraceptive Research and Development and create an Alliance for Contraceptive Development

Although our recommendations are diverse, all are interconnected and important for improving the range of products, their efficacies, and their acceptability.
FROM TARGET SELECTION TO PRODUCT DEVELOPMENT

In the course of genomics research, thousands of genes expressed in the reproductive cells and tissues of model organisms and humans have been identified, and many of these sequences appear to be unique to reproductive tissues and gametes. The identification of genes and proteins that are expressed specifically in the reproductive tract and, more importantly, that function specifically in the reproductive tract, could lead to the development of new contraceptives that specifically affect the reproductive tract and thus produce minimal unwanted side effects. Thus the committee recommended further research to identify genes and cellular components that are unique to reproductive processes and could serve as targets for new contraceptives.

To this end, the committee also recommended accelerating the discovery and development of compounds that modulate existing and emerging targets by using high-throughput drug discovery approaches. The effort will require a variety of experimental approaches, from in vitro studies to whole-animal studies, to evaluate lead molecules for the purpose of subsequent clinical development (translational research). The committee also emphasized the need to apply recent advances in drug delivery systems and the importance of accelerating and improving clinical testing of new contraceptive methods.

Researchers must remember to consider acceptability early in development, before investing a large effort into product development and clinical trials. They should also consider other possible associated benefits of contraceptive methods. For example, a contraceptive method that also confers protection against HIV infection and other STIs is likely to have widespread benefit.

STRATEGIES FOR RESEARCH SUCCESS

The committee concluded that the creation of public-private partnerships is an important mechanism to advance research in reproductive health and contraception. The complementary scientific strengths and focus of the not-for-profit and for-profit sectors are necessary to ensure rapid progress in the translation of lead compounds to products.

The committee also recommends increasing the participation of developing countries. Organizations in developing countries can make valuable contributions to contraceptive development in many ways, including playing a role in assessing contraceptive acceptability among users, and by their active research programs and flourishing pharmaceutical industries.

Another strategy for research success involves increasing clinical and scientific training and career development in contraception. A major challenge is to identify, attract,
train, and support the career development of young investigators in basic, translational, clinical, and social sciences and project management who have an interest in and appreciation for the multidisciplinary issues surrounding fertility regulation. More postdoctoral training opportunities are needed, and trainees who complete a rigorous program should be recognized as experts through learned societies or organizations. To encourage young investigators, there must also be the promise of adequate opportunities to obtain research funding.

Finally, the committee recommended a number of ways to improve communication among the many parties with an interest in this rapidly changing scientific field including an international alliance, with a shared database of information, and a Forum on Contraceptive Research to provide a mechanism to facilitate integration of the activities of different stakeholders.

CONCLUSION

The development of new contraceptives benefits men, women, and families worldwide because contraception is one of the most effective means of improving reproductive health and quality of life. The extraordinary recent advances in science and technology provide unprecedented opportunities to develop completely new approaches to contraception. Now is the time to address the critical needs and issues identified in this report and to ensure that future investments in contraceptive research, discovery, and development are brought to fruition to improve the lives and health of people worldwide. Although the committee’s recommendations are diverse, all are interconnected and important for improving the range of products, their efficacies, and their acceptability. It is the committee’s hope that sponsors, both public and private, will find topics of interest among this menu of research goals.

For More Information...

Copies of New Frontiers in Contraceptive Research: A Blueprint for Action are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, http://www.nap.edu. The full text of this report will be available at http://www.nap.edu

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

Support for this project was provided by The Bill and Melinda Gates Foundation. The views presented in this report are those of the Institute of Medicine Committee on New Frontiers in Contraceptive Research and are not necessarily those of the funding agencies. For more information about the Institute of Medicine, visit the IOM home page at: www.iom.edu.

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