CLOMIPHENE

A 3-IN-1 MEDICAL REFERENCE

Medical Dictionary

Bibliography &

Annotated Research Guide

TO INTERNET REFERENCES

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CLOMIPHENE

A MEDICAL DICTIONARY, BIBLIOGRAPHY,
AND ANNOTATED RESEARCH GUIDE TO
INTERNET REFERENCES

JAMES N. PARKER, M.D.
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The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this book which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which produce publications on clomiphene. Books in this series draw from various agencies and institutions associated with the United States Department of Health and Human Services, and in particular, the Office of the Secretary of Health and Human Services (OS), the Administration for Children and Families (ACF), the Administration on Aging (AOA), the Agency for Healthcare Research and Quality (AHRQ), the Agency for Toxic Substances and Disease Registry (ATSDR), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Healthcare Financing Administration (HCFA), the Health Resources and Services Administration (HRSA), the Indian Health Service (IHS), the institutions of the National Institutes of Health (NIH), the Program Support Center (PSC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition to these sources, information gathered from the National Library of Medicine, the United States Patent Office, the European Union, and their related organizations has been invaluable in the creation of this book. Some of the work represented was financially supported by the Research and Development Committee at INSEAD. This support is gratefully acknowledged. Finally, special thanks are owed to Tiffany Freeman for her excellent editorial support.

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In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with clomiphene is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about clomiphene, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to clomiphene, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on clomiphene. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to clomiphene, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on clomiphene.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON CLOMIPHENE

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on clomiphene.

Federally Funded Research on Clomiphene

The U.S. Government supports a variety of research studies relating to clomiphene. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to clomiphene.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore clomiphene. The following is typical of the type of information found when searching the CRISP database for clomiphene:

- **Project Title: ANTIESTROGENIC EFFECTS ON TUMOR ANGIOGENESIS**

  Principal Investigator & Institution: Blackwell, Kimberly L.; Medicine; Duke University Durham, Nc 27710

  Timing: Fiscal Year 2002; Project Start 01-MAY-2001; Project End 30-APR-2006

  Summary: (provided by Applicant) Tamoxifen, an estrogen receptor (ER) ligand, is the most commonly used drug for the treatment and prevention of breast cancer. Other ER-

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

modulating drugs include pure ER antagonists, such as ICI 182,780, and selective ER modulators (SERMs) such as raloxifene, idoxifene, **clomiphene** and GW 7604. These drugs have traditionally been thought to act through interaction with the estrogen receptor, and therefore, the secondary ER-independent mechanisms and alternative effects of these drugs are just being discovered. The primary aim of this grant is to examine the effects of antiestrogenic drugs on the most important cell type involved in angiogenesis, the vascular endothelial cell. Three approaches will examine these effects. The first approach will utilize animal models (corneal pocket assay, dorsal skin-fold windows) to quantify angiogenesis in several tumor types treated with various estrogen receptor modulating drugs. The second approach will isolate and identify a newly described tamoxifen binding site in endothelial cells. Drug interactions with this site appear to be related to endothelial cell toxicity and apoptosis. The third approach will examine cellular events in endothelial cells that are affected by estrogen receptor modulation including migration, calcium signaling, nitric oxide production, and protein transcriptional regulation. All proposed approaches will use a number of mechanistically different estrogen receptor modulators, including tamoxifen, 4-OH tamoxifen, raloxifene, idoxifene, ICI 182,780, GW 7604, and **clomiphene.** All approaches will employ both estrogen receptor positive (ER+) and estrogen receptor negative (ER-) cancer cell lines and a variety of endothelial cell lines. In addition, this proposal investigates the time frame of action for each observed effect. By examining the time course of actions of each mechanistically different drug, the difference between genomic and non-genomic actions can be ascertained. By identifying and characterizing a new tamoxifen binding site, and further defining ER-independent actions of antiestrogens on endothelial cells that are mediated by this binding site, novel therapeutics can be developed which prevent tamoxifen resistance, reduce thromboembolic complications, and are more effective in inhibiting tumor angiogenesis. The results of this project will have profound implications, especially as clinicians begin to use the newer estrogen receptor modulating drugs for the prevention and treatment of breast cancer.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: COOPERATIVE MULTICENTER REPRODUCTIVE MEDICINE NETWORK**

  Principal Investigator & Institution: Legro, Richard S.; Associate Professor; Obstetrics-Gynecology; Pennsylvania State Univ Hershey Med Ctr 500 University Drive Hershey, Pa 170332390

  Timing: Fiscal Year 2002; Project Start 30-JUN-2000; Project End 31-MAR-2005

  Summary: The overall hypothesis of this proposal is that insulin resistance is the fundamental pathophysiologic defect in women with polycystic ovary syndrome (PCOS), and therefore interventions to improve it are most likely to result in spontaneous ovulation and a singleton term pregnancy in infertile PCOS women. The primary aim is to identify the most effective form of ovulation induction in PCOS women that will result in a full term singleton intrauterine pregnancy with the safest profile. We propose to perform a multicenter-randomized trial of two methods of ovulation induction in clomiphene-resistant PCOS women (failure to either ovulate or conceive after an adequate trial of clomiphene). The women will be randomized to either gonadotropin or metformin treatment. Gonadotropins are the current standard method of ovulation induction in **clomiphene** resistant PCOS women and directly stimulate ovarian follicular development. The large cohort of arrested antral follicles and the unique pathophysiology of insulin resistance in PCOS places these women at particular risk for ovarian hyperstimulation syndrome (OHSS) and multiple pregnancy

with this form of therapy. Metformin achieves ovulation through improvement in insulin sensitivity and suppression of hepatic gluconeogenesis. These changes induce secondary effects of decreased circulating insulin, androgens and gonadotropins, increased sex hormone binding globulin, and increased ovulatory function. PCOS women will be identified on the basis of unexplained hyperandrogenemic chronic anovulation, without other health problems, and no other major infertility factor. We hypothesize that the treatment arm that improves insulin sensitivity will be more likely to result in monofollicular ovulation and thus singleton pregnancy, and less likely to result in the complications of ovulation induction including multiple pregnancy and OHSS. This study could have a major impact on infertility in PCOS women while avoiding the risks and costly burden of OHSS and multiple pregnancy.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EFFECTS CHRONIC INSULIN REDUCTION SPONTANEOUS AND INDUCED OVULATION**

  Principal Investigator & Institution: Ratts, Valerie; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2002

  Summary: There is no text on file for this abstract.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EFFECTS OF DECREASED HYPERINSULINEMIA ON THE OVULATORY RESPONSE TO CLOMIPHENE**

  Principal Investigator & Institution: Evans, William S.; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

  Timing: Fiscal Year 2002

  Summary: This abstract is not available.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INSULIN AND OVARIAN/METABOLIC RESPONSES IN PCOS**

  Principal Investigator & Institution: Nestler, John E.; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

  Timing: Fiscal Year 2002

  Summary: The polycystic ovary syndrome (PCOS) is a major health problem that affects approximately 6% of women of reproductive age. PCOS is characterized by hyperandogenism and anovulation, and is the leading cause of female infertility in the United States. Evidence suggests that insulin resistance accompanies by compensatory hyperinsulinemia is a common features of PCOS, and that hyperinsulinemia is responsible in part for the hyperandrogenism of the disorder. However, clinical studies have not assessed the possible role of hyperinsulinemia in promoting the chronic anovulation of PCOS, nor have they examined whether improving insulin selectivity alters PCOS-associated morbidities that may also be linked to insulin resistance and/or hyperinsulinemia, such as glucose intolerance, hypertension, dyslipidemia and atherosclerosis. Therefore, we propose 1) to assess the effects of chronic (12 month) insulin reduction on the hormonal, metabolic (glucose tolerance, blood pressure, lipids, PAI-1, tPA antigen) and ovulatory profiles of women with PCOS, as well as the time course of any changes, 2) to determine whether pharmacologically improving the insulin sensitivity of clomiphene-resistant PCOS women increase the rates of

spontaneous and/or clomiphene-induced ovulation, and 3) to determine whether hyperinsulinemia alters 24 hours before and after administration of **clomiphene** plus placebo or metformin). If our studies confirm an important role of hyperinsulinemia in the pathogenesis of PCOS, they have significant practical implications. That is, they will provide compelling evidence that the first-line treatment of anovulation due to PCOS should be measured aimed at improving insulin sensitivity and reducing serum insulin--including the use of "insulin-sensitizing" agents. Moreover, they will suggest that in women who have failed standard ovulation induction measures, the relatively inexpensive and non-invasive technique of "insulin sensitization" should be employed prior to the initiation of expensive and more complicated technology. Finally, our findings should reveal whether insulin sensitization beneficially affects PCOS co-morbidities that may also be related to insulin resistance or hyperinsulinemia.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INTRATESTICULAR TESTOSTERONE AND SPERMATOGENESIS IN MAN**

  Principal Investigator & Institution: Zirkin, Barry R.; Professor; Biochem and Molecular Biology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2004; Project Start 01-FEB-2004; Project End 30-NOV-2008

  Summary: (provided by applicant): It is well established for both rat and man that the total testosterone concentration within the testes is far higher than that in serum. We know for the that intratesticular testosterone can be reduced by 50-60% without effect on spermatogenesis, but that the required testosterone concentration is still 10-fold greater than serum testosterone concentration. This kind of information, if available for the human, could prove invaluable for understanding and treating at least subsets of men with infertility. Unfortunately, we know little about the androgen content of intratesticular fluid within the human testis or the relationship between intratesticular androgens and human spermatogenesis. Our recent studies of the human have demonstrated that, as in the rat, there is a gradient between the concentration of testosterone in serum and within the testis; intratesticular testosterone levels were found to be 100-fold higher than normal serum testosterone levels. We do not yet know how much of the testosterone within the human testis is required either to maintain or restore quantitatively normal spermatogenesis because, as yet, experimental studies comparable to those performed in the rat have not been feasible for the human. Moreover, we know little about the concentration of bioavailable androgens within the testes of any mammal, and therefore virtually nothing about the relationship between bioavailable androgen concentration and spermatogenesis in rat or man. The major objectives of this project are to identify and quantify the androgen content of the human testis, to assess the bioavailability of intratesticular androgens, to experimentally determine the relationship between bioavailable intratesticular androgen concentration and spermatogenesis, and to examine the effect of testosterone replacement modalities on intratesticular bioavailable androgen concentration and on spermatogenesis in subfertile men.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: OPTIMAL INFERTILITY THERAPY RCT: WOMEN 40 AND OLDER**

  Principal Investigator & Institution: Reindollar, Richard H.; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-APR-2008

Summary: (provided by applicant): This study will determine the most effective treatment strategy for infertile couples who present when the female partner is 40-43 years old and are determined to have a reasonable chance for success. We will conduct a randomized clinical trial to compare success rates and costs. Eligible couples will be randomized to one of three treatment arms: four cycles of immediate in vitro fertilization (IVF), two cycles of clomiphene/intrauterine insemination (IUI) followed by four cycles of IVF, or two cycles of FSH/IUI followed by four cycles of IVF. Visits for infertility services by women of advanced reproductive age have increased disproportionately to those of younger women. Natural fecundity decreases markedly after age 40 because of a decrease in the number of viable oocytes within the ovaries and an increasing proportion of chromosomal abnormalities in those that remain. Success rates for fertility treatment using their own oocytes are significantly lower for older couples. However, for those with adequate ovarian function, achieving pregnancy may be possible before turning to alternative means of building a family. 1,500 deliveries were reported nationwide in the 1999 CDC National Summary and Fertility Clinics Report for this age group. Very few studies exist in conventional treatments that include the use of superovulation and IUI (SO/IUI) with either **clomiphene** (an oral medication) or injectable gonadotropins. Although it is likely that these treatments do not differ in success, an unproven bias exists against the less expensive of the two. No randomized trials comparing SO/IUI with IVF in older couples with a reasonable ovarian reserve have been performed. IVF success rates for these couples are higher than the rates reported from small studies using SO/IUI. The proposed study takes advantage of two local features: (1) BIDMC/Boston IVF is the largest infertility center in the United States, treating over 3,084 new patient couples each year, 509 of whom the female partner is 40-43, and performing nearly 6% of all US IVF procedures for this age group; and, (2) insurance coverage for infertility is required by Massachusetts law for all participants. The choice of therapeutic alternatives is unaffected by the patient's ability to pay for treatment.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: RACIAL DIFFERENCES IN CIRCULATING SEX STEROIDS**

  Principal Investigator & Institution: Bohler, Henry; Meharry Medical College 1005-D B Todd Blvd Nashville, Tn 37208

  Timing: Fiscal Year 2003; Project Start 10-JUL-2003; Project End 30-JUN-2008

  Summary: The overall hypothesis of this proposal is that elevated sex steroid levels may account for some of the hormone related conditions that follow throughout life in African American females, including leiomyomas, endocrine related cancers, and protection from osteoporosis. If so, we may then begin to understand their contribution to these processes, both protective and additive in Black females. This will form the basis for better understanding these conditions in all females, and also will allow us to amend our preventive strategies to prevent these morbidities. We propose to both quantify differences in sex steroid levels in the normal menstrual cycle, as well as to identify mechanisms. We further propose to examine the effects of sex steroids on an end organ-in this case bone mineral density and architecture.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ROSIGLITAZONE AND CLOMIPHENE FOR OVULATION INDUCTION**

  Principal Investigator & Institution: Cataldo, Nicholas A.; Assistant Professor of Obstetrics and Gy; Gynecology and Obstetrics; Stanford University Stanford, Ca 94305

Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2004

Summary: This proposal will evaluate the effectiveness of a new drug combination, rosiglitazone and **clomiphene,** for the induction of ovulation in anovulatory women with polycystic ovary syndrome (PCOS). PCOS is a disorder affecting about 5% of women of reproductive age, characterized by anovulation with loss of menstrual cyclicity and hyperandrogenism, often resulting in hirsutism or acne. Anovulation leads to spontaneous infertility and poses a risk of endometrial carcinoma if untreated. A majority of women with PCOS have peripheral insulin resistance and compensatory hyperinsulinemia. These abnormalities may lead to a long-term increased rish of Type 2 diabetes mellitus, hypertension, and accelerated atherosclerosis. Induction of ovulation is necessary to restore fertility to women with PCOS. The standard initial treatment is oral **clomiphene** citrate, a selective estrogen-receptor modulator which increases endogenous FSH secretion. **Clomiphene** is successful in inducing ovulation in only about 70% of women with PCOS, and failure is associated with hyperinsulinemia. Women who fail **clomiphene** ovulation induction are usually treated with parenteral FSH, but this is associated with a greater risk than **clomiphene** of both multiple gestation and ovarian hyperstimulation syndrome, which in its severe form can be life-threatening. This study will examine whether **clomiphene** can be more effective in inducing ovulation in women with PCOS when given concomitantly with rosiglitazone, an insulin sensitizer which lowers circulating insulin levels. Women with PCOS selected for previous resistance to **clomiphene** ovulation induction will be randomized to receive either rosiglitazone or placebo in double-bind fashion for 6 weeks, and then will undergo attempted ovulation induction with **clomiphene.** If unsuccessful, the **clomiphene** dose will be increased in up to 2 subsequent cycles in standard fashion in an effort to achieve ovulation. Spontaneous and clomiphene-induced ovulatory outcomes, assessed by serum progesterone levels, will be compared between rosiglitazone and placebo groups and correlated with changes in hyperinsulinemia, assessed on oral glucose tolerance testing (OGTT), and with changes in baseline LH, total and free testosterone, sex hormone binding globulin (SHBG), and insulin-like growth factor binding protein-1 (IGFBP-1) levels. The effects of rosiglitazone on insulin secretion on OGTT will be correlated with its effects on the levels of the above hormones and binding proteins.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[3] The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

[3] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

To generate your own bibliography of studies dealing with clomiphene, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "clomiphene" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for clomiphene (hyperlinks lead to article summaries):

- **A clomiphene citrate and tamoxifen citrate combination therapy: a novel therapy for ovulation induction.**
  Author(s): Suginami H, Kitagawa H, Nakahashi N, Yano K, Matsubara K.
  Source: Fertility and Sterility. 1993 May; 59(5): 976-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8486198

- **A comparison of clomiphene citrate and human menopausal gonadotropin for use in conjunction with intrauterine insemination.**
  Author(s): Manganiello PD, Stern JE, Stukel TA, Crow H, Brinck-Johnsen T, Weiss JE.
  Source: Fertility and Sterility. 1997 September; 68(3): 405-12.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9314905

- **A cost comparison of infertility treatment for clomiphene resistant polycystic ovary syndrome.**
  Author(s): Fridstrom M, Sjoblom P, Granberg M, Hillensjo T.
  Source: Acta Obstetricia Et Gynecologica Scandinavica. 1999 March; 78(3): 212-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10078583

- **A dopamine D3 receptor genotype is associated with hyperandrogenic chronic anovulation and resistant to ovulation induction with clomiphene citrate in female Hispanics.**
  Author(s): Legro RS, Muhleman DR, Comings DE, Lobo RA, Kovacs BW.
  Source: Fertility and Sterility. 1995 April; 63(4): 779-84.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7890062

- **A nomogram to predict the probability of live birth after clomiphene citrate induction of ovulation in normogonadotropic oligoamenorrheic infertility.**
  Author(s): Imani B, Eijkemans MJ, te Velde ER, Habbema JD, Fauser BC.
  Source: Fertility and Sterility. 2002 January; 77(1): 91-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11779596

- **A prospective comparative trial of a gonadotropin-releasing hormone analogue with clomiphene citrate for the treatment of oligoasthenozoospermia.**
  Author(s): Matsumiya K, Kitamura M, Kishikawa H, Kondoh N, Fujiwara Y, Namiki M, Okuyama A.
  Source: International Journal of Urology : Official Journal of the Japanese Urological Association. 1998 July; 5(4): 361-3.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9712445

- **A prospective evaluation of clomiphene citrate challenge test screening of the general infertility population.**
  Author(s): Scott RT, Leonardi MR, Hofmann GE, Illions EH, Neal GS, Navot D.
  Source: Obstetrics and Gynecology. 1993 October; 82(4 Pt 1): 539-44.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8377979

- **A prospective randomized trial of artificial insemination versus intercourse in cycles stimulated with human menopausal gonadotropin or clomiphene citrate.**
  Author(s): Karlstrom PO, Bergh T, Lundkvist O.
  Source: Fertility and Sterility. 1993 March; 59(3): 554-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8458457

- **A prospective, double-blind, randomized, placebo-controlled clinical trial of bromocriptin in clomiphene-resistant patients with polycystic ovary syndrome and normal prolactin level.**
  Author(s): Parsanezhad ME, Alborzi S, Namavar Jahromi B.
  Source: Archives of Gynecology and Obstetrics. 2004 January; 269(2): 125-9. Epub 2002 October 24.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14648180

- **A prospective, double-blind, randomized, placebo-controlled clinical trial of bromocriptine in clomiphene-resistant patients with polycystic ovary syndrome and normal prolactin level.**
  Author(s): Parsanezhad ME, Alborzi S, Jahromi BN.
  Source: Int J Fertil Womens Med. 2002 November-December; 47(6): 272-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12570169

- **A randomized clinical trial of treatment of clomiphene citrate-resistant anovulation with the use of oral contraceptive pill suppression and repeat clomiphene citrate treatment.**
  Author(s): Branigan EF, Estes MA.
  Source: American Journal of Obstetrics and Gynecology. 2003 June; 188(6): 1424-8; Discussion 1429-30.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12824973

- **A randomized controlled trial of laparoscopic ovarian diathermy versus gonadotropin therapy for women with clomiphene citrate-resistant polycystic ovary syndrome.**
  Author(s): Farquhar CM, Williamson K, Gudex G, Johnson NP, Garland J, Sadler L.
  Source: Fertility and Sterility. 2002 August; 78(2): 404-11.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12137881

- **A randomized double-blind comparison of perifollicular vascularity and endometrial receptivity in ovulatory women taking clomiphene citrate at two different times.**
  Author(s): Cheung W, Ng EH, Ho PC.
  Source: Human Reproduction (Oxford, England). 2002 November; 17(11): 2881-4.
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