

WHO Updates Medical Eligibility Criteria for Contraceptives



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The World Health Organization (WHO) has issued new family planning guidance, including the following:

- Most women with HIV infection generally can use IUDs.
- Women generally can take hormonal contraceptives while on antiretroviral (ARV) therapy for HIV infection, although there are interactions between contraceptive hormones and certain ARV drugs.
- Women with clinical depression usually can take hormonal contraceptives.

More than 35 experts met at WHO headquarters in Geneva, Switzerland, in October 2003 and developed this and other new guidance. The new guidance updates the Medical Eligibility

Criteria (MEC) for Contraceptive Use. This was the third expert meeting to consider medical eligibility criteria. WHO first issued the MEC in 1996; they were first updated in 2000 (51).

MEC help define who can use which contraceptive methods

The MEC offer guidance on whether a person with a specific health condition can safely start to use a specific contraceptive method or, if she or he develops a health condition, can continue to use the method safely. For each health condition and contraceptive method addressed, the Expert Working Group by consensus classified a condition on a scale of 1 to 4. Table 1 describes these four categories, which were set out at the first

MEC meetings in 1994-95. Where limited clinical judgement is available, categories 1 and 2 mean that people with the specific condition can safely use the method; categories 3 and 4 mean that they should not use it.

In the 2003 meeting the Expert Working Group addressed contraceptive use in situations involving or related to HIV/AIDS, considered whether certain drugs interact with hormonal contraceptives, assessed several new contraceptive methods, looked at several new conditions, and reviewed new evidence relevant to several other issues. This issue of *INFO Reports* focuses on changes and new criteria likely to have the greatest impact on service delivery. ❖

Table 1. WHO Medical Eligibility Criteria Classifications

Category	Description	Interpretation When Clinical Judgement Is Available	Interpretation When Clinical Judgement Is Limited
1	No restriction for the use of the contraceptive method.	Use the method in any circumstances.	Use the method.
2	The advantages of using the method generally outweigh the theoretical or proven risks.	Generally use the method.	
3	The theoretical or proven risks usually outweigh the advantages of using the method. Safe use requires careful clinical judgement and access to clinical services.	Use of method not usually recommended unless other more appropriate methods are not available or not acceptable.	Do not use the method.
4	A condition which represents an unacceptable health risk if the contraceptive method is used.	Method not to be used.	

Source: World Health Organization, 2000 (51)

Women with HIV infection generally can use IUDs

The 2003 Expert Working Group made several changes to the MEC to indicate that women often can safely use IUDs in conditions related to HIV and other sexually transmitted infections (STIs). Taken together, these changes should help reduce some providers' concerns about offering IUDs in areas where HIV infection and other STIs are common.

At the meeting the WHO Expert Working Group concluded that a woman generally can start using an IUD, if she wishes, even if she has AIDS—provided she is receiving ARV therapy and is clinically well—or if she has HIV infection or she is at high risk of HIV infection. The Expert Working Group changed these conditions from category 3 to category 2 for starting IUD use (see Table 2). According to the bulk of research considered at the WHO meeting, IUD use does not increase a woman's chances of acquiring HIV infection (2, 3, 14, 15, 22-24, 35, 37, 39, 43).

Women generally can keep their IUDs if they become infected with HIV or develop AIDS while using IUDs (category 2), although IUD users with AIDS should be carefully monitored for pelvic infection. Limited evidence shows that complications of IUD use are no more common among IUD users infected with HIV than among IUD users who are not infected with HIV (29, 40). Also, IUD use does not increase HIV transmission to sexual partners (2, 30, 38).

IUD generally can stay during treatment for STI or PID

Concerning other STIs, the WHO Expert Working Group concluded that a woman generally can keep her IUD (category 2) even if she develops an STI or pelvic inflammatory disease (PID) while using the method, provided the infection is successfully treated. The shift to category 2 makes the MEC consistent with WHO's Selected Practice Recommendations concerning PID and IUDs, issued in 2002 (52). These changes rest on findings that there is no difference in the clinical course of PID whether the IUD is removed or left in place during treatment (18, 42, 45). Furthermore, a woman usually can start IUD use even if she has an STI other than chlamydial infection or gonorrhea (category 2). These other STIs include ulcerative diseases such as syphilis and herpes.

After considering evidence on IUD use in situations where STIs are common, the Expert Working Group concluded that a woman can usually have an IUD inserted unless she faces a very high *individual* likelihood of exposure to chlamydia or gonorrhea. A study in Kenya found that women at high individual risk of these STIs were more likely to develop IUD-related complications after the device was inserted than those not at high risk (28). The Expert Working Group distinguished individual likelihood of exposure from high prevalence of these STIs in an area.

A provider still usually should not insert an IUD in a woman known to have AIDS (category 3) unless she is clinically well on ARV therapy (category 2). Nor should a woman receive an IUD if she has PID, chlamydial infection, gonorrhea, or purulent cervi-

tis (category 4). The MEC meeting did not change these classifications. Chlamydial infection and gonorrhea can manifest themselves as purulent cervicitis.

For two other conditions—obesity, and uterine fibroids that do not distort the uterine cavity—the Expert Working Group saw no evidence supporting a need for restrictions on IUD use (see Table 2).

Women on antiretroviral therapy generally can use hormonal contraceptives

In light of perhaps 1 million people worldwide now using antiretroviral (ARV) therapy for HIV and a United Nations goal of treating 3 million, about half of whom will be women, by

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the end of 2005 (54), the MEC meeting assessed whether and how ARV drugs and contraceptive hormones interact. The chief concern is that ARV drugs might reduce the effectiveness of hormonal contraceptives and so increase the risk of pregnancy.

The few pharmacokinetic studies of certain ARV therapies used with limited courses of combined oral contraceptives (COCs) showed both positive and negative effects on hormone levels, and so the Expert Working Group expressed caution by categorizing hormonal contraceptives a Category 2 for users of ARV therapy. The evidence is not sufficient, however, to conclude that women on ARV therapy should avoid hormonal contraceptives. No studies of actual clinical outcomes, such as pregnancy rates or indicators of ovulation, have been completed. Thus there is not sufficient evidence yet whether or not the effectiveness of either hormonal contraceptives or ARV therapy is compromised. Clinical and pharmacokinetic studies involving the injectable progestin depot medroxyprogesterone acetate (DMPA) (*Depo-Provera*[®]) are underway. Concern about lessened contraceptive effectiveness would focus, however, on lower-dose methods, such as COCs and progestin-only pills, and not so much on injectables. A woman who is infected with HIV should use condoms to prevent HIV transmission and to avoid reinfection. Consistent and correct use of condoms may compensate for any decrease in the effectiveness of hormonal methods (53).

Experts do not expect several classes of ARV drugs to interact with hormones because ARV drugs in these classes appear to have no effect on liver enzymes. Such drugs include nucleoside reverse transcriptase inhibitors (NRTIs) such as zidovudine,

Table 2. IUDs: Medical Eligibility Criteria Considered by the 2003 WHO Expert Working Group

Condition	Method			
	Cu-IUD		LNG-IUD	
	Initiation	Continuation	Initiation	Continuation
<i>PID—current*</i>	4	3 → 2 ^a	4	3 → 2 ^a
STIs				
a) <i>Current purulent cervicitis or chlamydial infection or gonorrhea**</i>	4	4 → 2 ^a	4	4 → 2 ^a
b) <i>Other STIs (excluding HIV and hepatitis)</i>	2	2	2	2
c) <i>Vaginitis (including trichomonas vaginalis and bacterial vaginosis)</i>	2	2	2	2
d) Increased risk of STIs	3 → 2/3 ^b	3 → 2	3 → 2/3 ^b	3 → 2
High risk of HIV	3 → 2	3 → 2	3 → 2	3 → 2
<i>HIV-infected†</i>	3 → 2	3 → 2	3 → 2	3 → 2
AIDS	3	3 → 2 ^c	3	3 → 2 ^c
<i>Clinically well on ARV therapy</i>	2	2	2	2
Uterine fibroids that do not distort the uterus	2 → 1	2 → 1	2 → 1	2 → 1
Obesity	1	1	2 → 1	1

Source: World Health Organization, 2003 (55)
Refer to Table 1 for category definitions.

Conventions used in the tables of this report:

➔ Indicates that category changed in 2003 MEC meeting; previous category is shown to the left of the arrow; new category, to the right.

Italics on condition and categories indicate a new condition added to the MEC. *Italics* on condition only indicate a redefined condition; see specific footnote for explanation of change.

Shading in a cell of the table indicates that the current classification is category 3 (usually do not use) or 4 (do not use).

Cu-IUD = copper-bearing IUD

LNG-IUD = levonorgestrel-releasing IUD

*Formerly, “PID—current or within the last 3 months” (51)

**Formerly, STI “current or within 3 months (including purulent cervicitis)” (51)

†Formerly, “HIV-positive” (51)

Clarifications:

^a“Treat the PID/STI using appropriate antibiotics. There is usually no need for removal of the IUD if the client wishes to continue its use.” (55)

^b“If a woman has a very high individual likelihood of exposure to gonorrhea or chlamydia, the condition is a Category 3.” (55)

^c“IUD users with AIDS should be closely monitored for pelvic infection.” (55)

stavudine, and lamivudine; nucleotide reverse transcriptase inhibitors (NtRTIs) such as tenofovir; and fusion inhibitors such as enfurvitide (31). Evidence is insufficient, however, to conclude that no interactions exist between these classes of drugs and contraceptive hormones.

Concerns focus on non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as nevirapine and efavirenz and protease inhibitors such as saquinavir and ritonavir. Concerning the effectiveness of hormonal contraceptives, the few published pharmacokinetic studies of drug levels find conflicting effects on hormone levels after a single dose of COC hormones (25, 26, 36, 44). Concerning the effectiveness of ARV drugs, package labeling indicates that the level of the ARV drug amprenavir decreases when taken along with contraceptive hormones, while a study found levels of saquinavir unchanged. Currently, no more than one study report is available on any one ARV drug. For many ARV drugs no studies are available.

The ARV therapies proposed by WHO for use in limited-resource settings consist of two NsRTIs—lamivudine plus either stavudine or zidovudine—and an NNRTI—either nevirapine or efavirenz (53).

Hormonal methods again judged appropriate with high HIV risk, HIV, or AIDS

In another deliberation related to HIV/AIDS, the Expert Working Group concluded that evidence does not support any restrictions on hormonal contraceptives for women at high risk of HIV infection or with HIV infection, including those with AIDS. These health conditions remain category 1 for all hormonal methods. Exceptions are (1) initiation of the levonorgestrel-releasing IUD (category 3), where the concern is with insertion in women with AIDS, not with the hormone, and (2) ARV therapy (category 2/3; see previous section).

Hormonal methods do not protect against HIV infection. Condoms are the only family planning method that helps prevent HIV/AIDS and other STIs, as WHO guidance emphasizes (44).

Spermicide not suitable with high HIV risk, HIV, or AIDS

A 2001 meta-analysis of five studies concluded that women who use the spermicide nonoxynol-9 several times a day—usually sex workers—may be more likely to develop HIV infection than women who have sex just as often but do not use spermicide. When used this often, spermicide contributes to abrasions of the vaginal wall, perhaps making it easier for the AIDS-causing virus to enter vaginal tissue. For all women studied, most of whom had sex far less often than sex workers, the association between spermicide use and HIV infection was not statistically significant, but risk increased with frequency of use (49).

This evidence, which included a randomized controlled trial conducted by UNAIDS (47), moved the 2003 MEC meeting to reclassify spermicide to category 4 (not to be used) and diaphragms used with spermicide to category 3 (usually not recommended) for the conditions related to HIV/AIDS (see Table 3). ❖

Table 3. Spermicide: Medical Eligibility Criteria Considered by the 2003 WHO Expert Working Group

Condition	Method	
	Spermicide	Diaphragm*/ Cervical Cap
High risk of HIV	2 → 4	1 → 3
HIV-infected**	2 → 4	1 → 3
AIDS	2 → 4	1 → 3

Source: World Health Organization, 2003 (55)
Refer to Table 1 for category definitions.

*Used with spermicide
** Formerly, “HIV-positive”

Hormonal Methods Appropriate for Women with Depression

Considering depressive disorders for the first time, the October 2003 MEC meeting concluded that there is no need for restriction on use of hormonal contraceptives for women with depression (see Table 4). A variety of studies have found no increase in

symptoms among depressed women using combined or progestin-only oral contraceptives (5, 6, 10, 17), DMPA injectable (5, 8, 48), or *Norplant*[®] implants (5, 48). A single study reported that taking fluoxetine (*Prozac*[®]) for depression did not reduce the

effectiveness of combined or progestin-only oral contraceptives (17). Conclusions cannot be reached concerning postpartum depression or bipolar disorder because current evidence is inadequate (33). ❖

Table 4. Other New or Redefined Conditions Considered by the 2003 WHO Expert Working Group

Condition	Method								
	COC/ Patch/ Ring	CIC	POP	DMPA NET-EN Injectables	LNG/ETG Implants	Cu-IUD		LNG-IUD	
						Initiation	Continuation	Initiation	Continuation
<i>Depressive disorders</i>	1	1	1	1	1	1	1	1	1
<i>Known thrombogenic mutations</i>	4 ^a	4 ^a	2 ^a	2 ^a	2 ^a	1 ^a	1 ^a	2 ^a	1 ^a
Drug Interactions									
<i>Antiretroviral therapy</i>	2 ^b	2 ^b	2 ^b	2 ^b	2 ^b	2/3 ^c	2 ^c	2/3 ^c	2 ^c
Drugs that affect liver enzymes									
a) <i>Rifampicin</i> *	3	3→2	3	2	3	1	1	1	1
b) Certain anticonvulsants**	3	3→2	3	2	3	1	1	1	1
Antibiotics (excluding rifampicin)									
<i>Griseofulvin</i>	3→2	3→1	3→2	2→1	3→2	1	1	1	1

Source: World Health Organization, 2003 (55)
Refer to Table 1 for category definitions.

*Formerly, "Certain antibiotics (rifampicin and griseofulvin)" (51)

**“(phenytoin, carbamazepine, barbiturates, primidone, *topiramate*, *oxcarbazepine*)” (55). (Italicized anticonvulsants were added October 2003.)

CIC=Combined Injectable Contraceptives

POP=Progestin-Only Pills

Clarifications:

^a“Routine screening is not appropriate because of the rarity of the condition and the high cost of screening” (54). As for all the MEC, the classifications refer to *known* conditions and do not necessarily imply that screening is necessary or advisable.

^b“Limited data...suggest drug interactions between many antiretrovirals (ARVs) and hormonal contraceptives, but there are currently no clinical outcome studies. Current concerns relate to efficacy and toxicity for both the hormonal contraceptive and the ARVs” (55).

^c“There is no known drug interaction between ARV therapy and IUD use. However, AIDS as a condition is classified as Category 3 for insertion and Category 2 for continuation unless the woman is clinically well on ARV therapy, in which case both insertion and continuation are classified as Category 2.”

Criteria Reaffirmed for Broad-spectrum Antibiotics and Hormonal Methods, Cervical Neoplasia and COCs, Breastfeeding and Progestins

Broad-spectrum anti- biotics—no restrictions

Case reports have raised suspicions that broad-spectrum antibiotics in general might lower the effectiveness of hormonal contraceptives. Still, studies find that various broad-spectrum antibiotics do not lower hormone levels and, with one early exception (13), they have found no evidence of ovulation. Pregnancy rates are similar among women taking COCs alone and women taking both COCs and

antibiotics (9, 12, 20). The 2003 Expert Working Group left broad-spectrum antibiotics in MEC category 1 (use in any circumstances).

The MEC previously categorized use of the antibiotics rifampicin and griseofulvin both as category 3 (not usually recommended) for most hormonal contraceptives because these drugs were thought to reduce contraceptive effectiveness. There are reports of pregnancies in users of hormonal contraceptives taking griseofulvin, and griseofulvin affects liver enzymes in mice, suggesting a possible impact on hormone metabolism. There are no published clinical or pharmacokinetic studies on interaction between griseofulvin and contraceptive hormones, however. The Expert Working Group reclassified use of griseofulvin to category 1 for users of combined or progestin-only injectables and category 2 (generally use) for users of other hormonal methods.

increases with duration of use of COCs or DMPA. The association is statistically significant after five years of use. Only limited evidence, however, addresses the question of whether CIN is more likely to progress in women who use hormonal contraceptives. The few studies comparing COC use among women with low-grade cervical lesions and use among women with high-grade lesions yield inconsistent findings (1, 11, 16, 27, 34, 46). One study followed up women with low-grade lesions and found that progression was significantly more common in COC users than nonusers (7).

Postpartum limit on progestin-only methods stays at six weeks for breastfeeding women

The Expert Working Group continued to recommend that women who are breastfeeding should generally not use progestin-only contraceptives (category 3) until six weeks postpartum. The systematic review of the evidence found no adverse effects of these methods on breastfeeding patterns and, while the evidence is more limited, no adverse effects on infant growth, development, or health when women using progestin-only methods started breastfeeding before six weeks postpartum (32). Lacking data on the effects of progestin in breast milk on the infant's brain and liver development, however, the Expert Working Group did not shorten the 6-week restriction. Still, as the Expert Working Group had noted in 2000 and reaffirmed in 2003, in many settings the morbidity and mortality risks of pregnancy are high, and progestin-only contraceptives may be one of the few types of methods widely available to breastfeeding women immediately postpartum (51). ❖

Concern about cervical lesions, but hormonal meth- ods generally can be used

The Expert Working Group kept cervical intraepithelial neoplasia (CIN), noninvasive lesions considered a precursor to cervical cancer, in MEC category 2 (generally use) for hormonal contraceptives except progestin-only pills, for which CIN is classed as category 1 (use in any circumstances). The category 2 rating, assigned in the first edition of the MEC, reflects "some concern that COCs enhance the progression of CIN to invasive disease, particularly with long-term use" (that is, greater than five years) (51). According to a 2002 meta-analysis of over 30 studies presented to the Expert Working Group (41), the risk of developing invasive cervical cancer or one of its more immediate precursors



WHO Family Planning Guidance on the Internet

Latest MEC

http://www.who.int/reproductive-health/publications/MEC_3/index.htm

Related guidance from WHO, the Selected Practice Recommendations for Contraceptive Use (SPR), appears at http://www.who.int/reproductive-health/publications/rhr_02_7/index.htm

Keep up on new evidence related to the MEC.

The online system CIRE—Continuous Identification of Research Evidence—identifies new research articles whose study objectives concern a topic addressed by WHO's MEC or SPR. CIRE screens emerging scientific literature so that WHO guidance can be updated. Any updates to current guidance appear in WHO's postings of the MEC or SPR on the World Wide Web (see above). Changes to classifications of the MEC or to the SPR are ordinarily made only following expert group meetings such as the October 2003 MEC meeting. Records of all articles that CIRE has identified can be searched at http://www.infoforhealth.org/cire/cire_pub.pl

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MEC for Patch and Ring Same as for Combined Pills; Implanon Implant MEC Same as for Norplant

The Expert Working Group incorporated three new contraceptive methods into the MEC—the combined hormonal contraceptive patch, the combined hormone-releasing vaginal ring, and the etonogestrel-releasing implant, *Implanon*®. The hormone levels and patterns typical of the patch and the ring are similar to those for COCs, as are the type and frequency of side effects reported in comparative studies. Therefore, the meeting concluded, MEC classifications applying to COCs can be assumed to apply to the patch and ring as well. There is no direct evidence concerning use of either method among women with health conditions. The meeting also assumed that the MEC classifications for the 5-year levonorgestrel implant *Norplant* can also apply to the 3-year etonogestrel implant *Implanon*.

The Expert Working Group reclassified implants and also progestin-only injectables and the levonorgestrel-releasing IUD as far as obesity is concerned. All were changed to category 1 (use in any circumstance) from category 2 (generally use). Research involving the progestin-only injectable *Depo-Provera* (DMPA) leaves unclear whether obese women have more health problems, including additional weight gain or more bleeding changes, than DMPA users of lower weight (4, 19, 21).

Since the October 2003 meeting new evidence has become available showing that the effectiveness of *Norplant* implants decreases after the fourth year of use for women weighing over 70 kg. ❖



Source of citations to research studies:

In this issue of *INFO Reports* the citations to research studies come from systematic reviews conducted on behalf of the WHO Secretariat for the October 2003 Expert Working Group meeting. The Expert Working Group considered this evidence in reaching its decisions about medical eligibility criteria.

In general, these systematic reviews selected reports that were:

- Found through searches of MEDLINE, PREMEDLINE, POPLINE, and/or similar bibliographic databases;
- Published in peer-reviewed journals between 1966, in most cases, and August 2003; and
- Reported studies, systematic reviews of studies, or meta-analyses that examined health outcomes associated with use of a contraceptive method among women with a specified health condition.

Kate Curtis, PhD, and Anshu Mohllajee, MPH, of the US Centers for Disease Control and Prevention; Kavita Nanda, MD, MHS, of Family Health International; Lori Bastian, MD, MPH, of Duke University; Mary E. Gaffield, MPH, PhD, of WHO; and Jennifer S. Smith, PhD, MPH, of the International Agency for Research on Cancer, conducted these systematic reviews.



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1. BRISSON, J., MORIN, C., FORTIER, M., ROY, M., BOUCHARD, C., LECLERC, J., CHRISTEN, A., GUIMONT, C., PENNAULT, F., and MEISELS, A. Risk factors for cervical intraepithelial neoplasia: Differences between low- and high-grade lesions. *American Journal of Epidemiology* 140(8): 700-710. 1994.
2. BRITISH MEDICAL ASSOCIATION. Comparison of female to male and male to female transmission of HIV in 563 stable couples. *European Study Group on Heterosexual Transmission of HIV. British Medical Journal* 304: 809-813. 1992.
3. CARAEL, M., VAN DE PERRE, P.H., LEPAGE, P.H., ALLEN, S., NSENGUMUREMYI, F., VAN GOETHEM, C., NTAHORUTABA, M., NZARAMBA, D., and CLUMECK, N. Human immunodeficiency virus transmission among heterosexual couples in Central Africa. *AIDS* 2(3): 201-205. 1988.
4. CONNOR, P.D., TAVERNIER, L.A., THOMAS, S.M., GATES, D., and LYTTON, S.M. Determining risk between Depo-Provera use and increased uterine bleeding in obese and overweight women. *Journal of the American Board of Family Practice* 15(1): 7-10. Jan-Feb. 2002.
5. CROMER, B., SMITH, R., BLAIR, J., DWYER, J., and BROWN, R. A prospective study of adolescents who choose among levonorgestrel implant (Norplant), medroxy progesterone acetate (Depo-Provera), or the combined oral contraceptive pill as contraception. *Pediatrics* 94(5): 687-694. 1994.
6. DEIGEN, J., DUYN, K., JANSEN, W., and KLITSIE, J. Use of monophasic, low-dose oral contraceptive in relation to mental functioning. *Contraception* 46(4): 359-367. 1992.
7. DUGGAN, M.A., MCGREGOR, S.E., STUART, G.C., MORRIS, S., CHANG-POON, V., SCHEPANSKY, A., and HONORE, L. The natural history of CIN I lesions. *European Journal of Gynaecological Oncology* 19(4): 338-344. 1998.
8. GUPTA, N., O'BRIEN, R., JACOBSEN, L.J., DAVIS, A., ZUCKERMAN, A., SUPRAN, S., and KULIG, J. Mood changes in adolescents using depot-medroxyprogesterone acetate for contraception: A prospective study. *Journal of Pediatric and Adolescent Gynecology* 14(2): 71-76. May 2001.
9. HELMS, S.E., BREDLE, D.L., ZAJIC, J., JARFOURA, D., RODELL, R.T., and KRISHNARAO, I. Oral contraceptive failure rates and oral antibiotics. *Journal of the American Academy of Dermatology* 36(5): 5-10. 1997.
10. HERZBERG, B.N., DRAPER, K.C., JOHNSON, A.L., and NICOL, G.C. Oral contraceptives, depression, and libido. *British Medical Journal* 3(773): 495-500. 1971.
11. HO, G.Y., BURK, R.D., KLEIN, S., KADISH, A.S., CHANG, C.J., PALAN, P., BASU, J., TACHEZY, R., LEWIS, R., and ROMNEY, S. Persistent genital human papillomavirus infection as a risk factor for persistent cervical dysplasia. *Journal of the National Cancer Institute* 87(18): 1365-1371. Sep. 1995.
12. HUGHES, B.R. and CUNLIFFE, W.J. Interactions between the oral contraceptive pill and antibiotics. [Comment]. *British Journal of Dermatology* 122(5): 717-718. 1990.
13. JOSHI, J.V., JOSHI, U.M., SANKHOLI, G.M., KRISHNA, U., MANDLEKAR, A., CHOWDHURY, V., HAZARI, K., GUPTA, K., SHETH, U.K., and SAXENA, B.N. A study of interaction of low-dose combination oral contraceptive with Ampicillin and Metronidazole. *Contraception* 22(6): 643-652. Dec. 1980.
14. KAPIGA, S.H., LYAMUYA, E.F., LWIHULA, G.K., and HUNTER, D.J. The incidence of HIV infection among women using family planning methods in Dar es Salaam, Tanzania. *AIDS* 12(1): 75-84. Jan. 1998.
15. KAPIGA, S.H., SHAO, J.F., LWIHULA, G.K., and HUNTER, D.J. Risk factors for HIV infection among women in Dar-es-Salaam, Tanzania. *Journal of Acquired Immune Deficiency Syndromes* 7(3): 301-309. Mar. 1994.
16. KJAEER, S.K., ENGHOLM, G., DAHL, C., BOCK, J.E., LYNDE, E., and JENSEN, O.M. Case-control study of risk factors for cervical squamous-cell neoplasia in Denmark. III. Role of oral contraceptive use. *Cancer Causes Control* 4(6): 513-519. 1993.
17. KOKE, S., BROWN, E., and MINER, C. Safety and efficacy of fluoxetine in patients who receive oral contraceptive therapy. *American Journal of Obstetrics and Gynecology* 187(3): 551-555. 2002.
18. LARSSON, B. and WENNERGREN, M. Investigation of a copper-intrauterine device (Cu-IUD) for possible effect on frequency and healing of pelvic inflammatory disease. *Contraception* 15: 143-149. 1977.
19. LEIMAN, G. Depo-medroxyprogesterone acetate as a contraceptive agent: its effect on weight and blood pressure. *American Journal of Obstetrics and Gynecology* 114(1): 97-102. Sep. 1972.
20. LONDON, B. and LOOKINGBILL, D. Frequency of pregnancy in acne patients taking oral antibiotics and oral contraceptives. *Archives of Dermatology* 130(3): 392-393. 1994.
21. MANGAN, S.A., LARSEN, P.G., and HUDSON, S. Overweight teens at increased risk for weight gain while using depot medroxyprogesterone acetate. *Journal of Pediatric and Adolescent Gynecology* 15(2): 79-82. Apr. 2002.
22. MANN, J.M., NZILAMBI, N., PIOT, P., BOSENSE, N., KALALA, M., FRANCIS, H., COLEBUNDERS, R.C., AZILA, P.K., CURRAN, J.W., and QUINN, T.C. HIV infection and associated risk factors in female prostitutes in Kinshasa, Zaire. *AIDS* 2(4): 249-254. Aug. 1988.
23. MARTIN, H.L., JR., NYANGE, P.M., RICHARDSON, B.A., LAVREYS, L., MANDALIYA, K., JACKSON, D.J., NDINYA-ACHOLA, J.O., and KREISS, J. Hormonal contraception, sexually transmitted diseases, and risk of heterosexual transmission of human immunodeficiency virus type 1. *The Journal of Infectious Diseases* 178(4): 1053-1059. Oct. 1998.
24. MATI, J.K., HUNTER, D.J., MAGGWA, B.N., and TUKEI, P.M. Contraceptive use and the risk of HIV infection in Nairobi, Kenya. *International Journal of Gynaecology and Obstetrics* 48(1): 61-67. Jan. 1995.
25. MAYER, K., POBLETE, R., HATHAWAY, B., PALIC, B., PILSON, R., SIEMON-HRYCZYK, P., and DECAPRARIIS, R. Efficacy, effect of oral contraceptives and adherence in HIV infected women receiving Fortovase (Saqinavir) soft gel capsule (SQV-SGC; FTV) thrice (TID) and twice (BID) daily regimens. Presented at the XIII International AIDS Conference, Durban, 2000. (Available: <http://www.iacon2000.org/abstract.asp?ID=TuPeB3226>, Accessed Feb. 20, 2004)
26. MILDVAN, D., YARRISH, R., MARSHAK, A., HUTMAN, H.W., MCDONOUGH, M., LAMSON, M., and ROBINSON, P. Pharmacokinetic interaction between nevirapine and ethinyl estradiol/norethindrone when administered concurrently to HIV-infected women. *Journal of Acquired Immune Deficiency Syndromes* 29(5): 471-477. Apr. 2002.
27. MORENO, V., BOSCH, F.X., MUNOZ, N., MEIJER, C.J., SHAH, K.V., WALBOOMERS, J.M., HERRERO, R., and FRANCESCHI, S. Effect of oral contraceptives on risk of cervical cancer in women with human papillomavirus infection: The IARC multicentric case-control study. *Lancet* 359(9312): 1085-1092. 2002.
28. MORRISON, C.S., SEKADDE-KIGONDU, C., MILLER, W.C., WEINER, D.H., and SINEI, S.K. Use of sexually transmitted disease risk assessment algorithms for selection of intrauterine device candidates. *Contraception* 59(2): 97-106. Feb. 1999.
29. MORRISON, C.S., SEKADDE-KIGONDU, C., SINEI, S.K., WEINER, D.H., KWOK, C., and KOKONYA, D. Is the intrauterine device appropriate contraception for HIV-1-infected women? *British Journal of Obstetrics and Gynaecology* 108(8): 784-790. 2001.
30. MOSTAD, S.B., OVERBAUGH, J., DEVANGE, D.M., WELCH, M.J., CHOCHAN, B., MANDALIYA, K., NYANGE, P., MARTIN, H.L., JR., NDINYA-ACHOLA, J., BWAYO, J.J., and KREISS, J.K. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. *Lancet* 350(9082): 922-927. Sep. 1997.
31. NANDA, K. Hormonal contraceptive use in women treated with antiretroviral drugs. Presented at the Expert Working Group meeting to update the "Medical eligibility criteria for contraceptive use", Geneva, Oct 21-24, 2003. Family Health International (FHI).
32. NANDA, K. Progestin-only contraceptives in lactating women < 6 weeks postpartum. [Systematic Review]. Presented at the Expert Working Group meeting to update the "Medical eligibility criteria for contraceptive use", Geneva, Oct 21-24, 2003. Family Health International (FHI).
33. NANDA, K. and BASTIAN, L. Hormonal contraception in women with depression. Presented at the Expert Working Group meeting to update the "Medical eligibility criteria for contraceptive use", Geneva, Oct 21-24, 2003. Family Health International (FHI).
34. NEGRINI, B.P., SCHIFFMAN, M.H., KURMAN, R.J., BARNES, W., LANNON, L., MALLEY, K., BRINTON, L.A., DELGADO, G., JONES, S., TCHABO, J.G., and ET AL. Oral contraceptive use, human papillomavirus infection, and risk of early cytological abnormalities of the cervix. *Cancer Research* 50(15): 4670-4675. Aug. 1990.
35. NICOLOSI, A., CORREA LEITE, M.L., MUSICCO, M., ARICI, C., GAVAZZENI, G., and LAZZARIN, A. The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: A study of 730 stable couples. *Italian Study Group on HIV Heterosexual Transmission. Epidemiology* 5(6): 570-575. Nov. 1994.
36. OUELLET, D., HSU, A., QIAN, J., LOCKE, C.S., EASON, C.J., CAVANAUGH, J.H., LEONARD, J.M., and GRANNEMAN, G.R. Effect of ritonavir on the pharmacokinetics of ethinyl oestradiol in healthy female volunteers. *British Journal of Clinical Pharmacology* 46(2): 111-116. Aug. 1998.
37. PLOURDE, P.J., PLUMMER, F.A., PEPIN, J., AGOKI, E., MOSS, G., OMBETTE, J., RONALD, A.R., CHEANG, M., D'COSTA, L., and NDINYA-ACHOLA, J.O. Human immunodeficiency virus type 1 infection in women attending a sexually transmitted diseases clinic in Kenya. *Journal of Infectious Diseases* 166(1): 86-92. Jul. 1992.
38. RICHARDSON, B.A., MORRISON, C.S., SEKADDE-KIGONDU, C., SINEI, S.K., OVERBAUGH, J., PANTELEEFF, D.D., WEINER, D.H., and KREISS, J.K. Effect of intrauterine device use on cervical shedding of HIV-1 DNA. *AIDS* 13(15): 2091-2097. Oct. 1999.
39. SINEI, S.K., FORTNEY, J.A., KIGONDU, C.S., FELDBLUM, P.J., KUYOH, M., ALLEN, M.Y., and GLOVER, L.H. Contraceptive use and HIV infection in Kenyan family planning clinic attendees. *International Journal of STD & AIDS* 7(1): 65-70. 1996.
40. SINEI, S.K., MORRISON, C.S., SEKADDE-KIGONDU, C., ALLEN, M., and KOKONYA, D. Complications of use of intrauterine devices among HIV-1-infected women. *Lancet* 351(9111): 1238-1241. Apr. 1998.
41. SMITH, J.S., GREEN, J., BERRINGTON DE GONZALEZ, A., APPLEBY, P., PETO, J., PLUMMER, M., FRANCESCHI, S., and BERAL, V. Cervical cancer and use of hormonal contraceptives: a systematic review. *Lancet* 361(9364): 1159-1167. Apr. 2003.
42. SODERBERG, G. and LINDGREEN, S. Influence of an intrauterine device on the course of an acute salpingitis. *Contraception* 24: 137-143. 1981.
43. SPENCE, M.R., ROBBINS, S.M., POLANSKY, M., and SCHABLE, C.A. Seroprevalence of human immunodeficiency virus type 1 (HIV-1) antibodies in a family-planning population. *Sexually Transmitted Diseases* 18(3): 143-145. 1991.
44. TACKETT, D., CHILD, M., AGARWALA, S., GEIGER, M., GERALDES, M., and O'MARA, E. Atazanavir: A summary of two pharmacokinetic drug interaction studies in healthy subjects. [Abstract]. Presented at the 10th Retrovirus Conference, Boston, MA, Feb. 10-14, 2003. (Available: <http://www.retroconference.org/2003/Abstract/Abstract.asp?AbstractID=649>, Accessed Feb. 20, 2004)
45. TEISALA, K. Removal of an intrauterine device and the treatment of acute pelvic inflammatory disease. *Annals of Medicine* 21(1): 63-65. Feb. 1989.
46. THOMAS, D.B., YE, Z., and RAY, R.M. Cervical carcinoma in situ and use of depot-medroxyprogesterone acetate (DMPA). WHO Collaborative Study of Neoplasia and Steroid Contraceptives. *Contraception* 51(1): 25-31. 1995.
47. VAN DAMME, L., RAMJEE, G., ALARY, M., VUYLSTEKE, B., CHANDEYING, V., REES, H., SIRIVONGRANGSON, P., MUKENGE-TSHIBAKA, L., ETTIENNE-TRAORE, V., UAHEOWITCHAI, C., KARIM, S.S., MASSE, B., PERRIENS, J., and LAGA, M. Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. *Lancet* 360(9338): 971-977. 2002.
48. WESTHOFF, C., TRUMAN, C., KALMUSS, D., CUSHMAN, L., DAVIDSON, A., RULIN, M., and HEARTWELL, S. Depressive symptoms and Depo-Provera. *Contraception* 57(4): 237-240. Apr. 1998.
49. WILKINSON, D., RAMJEE, G., THOLANDI, M., and RUTHERFORD, G. Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men (Cochrane review). *The Cochrane Library* (3). Oxford, Update Software. 2003.
50. WILKINSON, D., THOLANDI, M., RAMJEE, G., and RUTHERFORD, G.W. Nonoxynol-9 spermicide for prevention of vaginally acquired HIV and other sexually transmitted infections: Systematic review and meta-analysis of randomised controlled trials including more than 5000 women. *Lancet Infectious Diseases* 2: 613-617. Oct. 2002.
51. WORLD HEALTH ORGANIZATION (WHO). Improving access to quality care in family planning: Medical eligibility criteria for contraceptive use. 2nd ed. Geneva, WHO, 2001.
52. WORLD HEALTH ORGANIZATION (WHO). Selected practice recommendations for contraceptive use. Geneva, WHO Department of Reproductive Health and Research, 2002. 94 p.
53. WORLD HEALTH ORGANIZATION (WHO). Scaling up antiretroviral therapy in resource-limited settings: Treatment guidelines for a public health approach. [Revision Draft]. Geneva, 2003. 44 p. (Available: <http://www.who.int/hiv/pub/prev_care/en/WHO_ARV_Guidelines_Update.pdf>, Accessed Feb. 20, 2004)
54. WORLD HEALTH ORGANIZATION (WHO). Treating 3 million by 2005: making it happen: the WHO strategy: the WHO and UNAIDS global initiative to provide antiretroviral therapy to 3 million people with HIV/AIDS in developing countries by the end of 2005. Geneva, WHO, 2003. (Available: <http://www.who.int/3by5/publications/documents/en/Treating3millionby2005.pdf>, Accessed Feb. 20, 2004)
55. WORLD HEALTH ORGANIZATION (WHO). In: Improving access to quality care in family planning: Medical eligibility criteria for contraceptive use. [3rd ed.] Geneva, Nov. 2004.