DST-901 Combined Hormonal Contraceptives (CHCs)

This Decision Support Tool (DST) provides clinical guidance for the provision of Combined Hormonal Contraceptives (CHCs). It is meant to be used in concert with the Contraceptive Management: Assessment DST.

DEFINITION

Combined Hormonal Contraceptives (CHCs) are contraceptives containing both estrogen and progestin. Three types of CHCs are available in Canada:

- Oral contraceptive pills
- Transdermal contraceptive patch
- Intravaginal/intragenital contraceptive ring

INDICATIONS

For the purpose of Contraceptive Management Registered Nurse Certified Practice or RN(C), CHCs are indicated for any client who is seeking a reliable, reversible method of contraception (Hatcher et al., 2018). RN(C)s may independently prescribe,[1] dispense, and/or administer CHCs of a dosage less than or equal to 50 mcg of ethinyl estradiol per day (BCCNM, 2021, 2022).

ACTION

The primary method of action of CHCs is through the suppression of gonadotropins induced by the estrogen and progestin effects on the hypothalamic/pituitary axis, thereby inhibiting ovulation (Hatcher et al., 2018). Progestin supresses luteinizing hormone (LH) secretions, thereby eliminating the LH surge while estrogen suppresses follicle stimulating hormone (FSH) secretion, thereby decreasing follicular maturation (Hatcher et al., 2018). Other mechanisms of action may include the development of endometrial atrophy, making the endometrium unreceptive to implantation and cervical mucus changes that impede sperm transport (Hatcher et al., 2018).

PHARMACOKINETICS

Dose

The majority of CHCs contains ethinyl estradiol (EE) and a progestin in various doses and combinations (Hatcher et al., 2018). The amount of EE in CHCs vary and the amount and type of progestin vary and differ in potency and metabolic effect. A low-dose CHC preparation is preferred to provide effective contraception, acceptable cycle control, and the least amount of side effects for the individual (Hatcher et al., 2018). CHCs that provide a daily dose of 50 mcg or less of ethinyl estradiol are considered to be 'low-dose' (Black et al., 2017).

In 2021, a new plant-based estrogen called estetrol (also known as 'E4') (trade name - Nextstellis®) was added to the Canadian market (Fruzzetti et al., 2021).

Oral CHC Formulations

Oral CHCs are taken daily, at the same time each day. There is a range of different formulations of oral CHCs available, for example 21/7, 24/4, or extended use.

- Monophasic: Each tablet contains a fixed amount of estrogen and progestin
- Biphasic: Each tablet contains a fixed amount of estrogen and the amount of progestin increases in the second half of the cycle
- Triphasic: The amount of estrogen can be fixed or variable and the amount of progestin increases in three equal phases

Transdermal CHC Formulations

The transdermal patch is changed once a week for three weeks, followed by one week patch-free.

[1] *RN(C)s who have met the requirements to prescribe.*

Each transdermal patch contains ethinyl estradiol 0.6 mg and norelgestromin 6 mg. The transdermal patch releases approximately ethinyl estradiol 35 mcg and norelgestromin 200 mcg per 24 hours (Hatcher et al., 2018).

Intravaginal/Intragenital CHC Formulations

The intravaginal/intragenital ring is worn inside the vagina/internal genitalia for three weeks followed by one week ring-free.

Each intravaginal/intragenital ring delivers ethinyl estradiol 15 mcg/day and etonogestrel 120 mcg/day (Hatcher et al., 2018).

Onset

Peak serum concentrations of combined estrogen and progestin vary between products. Contraceptive benefits are realized within seven days of consistent and correct CHC use (Hatcher et al., 2018).

Counsel clients of timing of contraceptive initiation based on current best practice guidelines and individual circumstances. The *Quick Start Method* is considered the best practice recommendation for initiation (Hatcher et al., 2018).

CONSULT OR REFERRAL

RN(C)s are restricted to prescribing, dispensing, and/or administering CHCs to clients who classify as category 1 or 2 as defined by the *U.S. Medical Eligibility Criteria for Contraceptive Use* (Curtis et al., 2016). RN(C)s cannot independently prescribe, dispense, or administer CHCs to clients who are classified as a category 3 or 4 without an order (Curtis et al., 2016).

Relative Contraindications

As per *U.S. Medical Eligibility Criteria for Contraceptive Use*, Category 3 (Curtis et al., 2016).

Absolute Contraindications

As per *U.S. Medical Eligibility Criteria for Contraceptive Use*, Category 4 (Curtis et al., 2016).

RN(C)s must refer or consult with a physician or nurse practitioner for the following clients (WHO, 2015):

- Clients wanting to use CHCs in the presence of relative or absolute contraindications as defined by the *U.S. Medical Eligibility Criteria for Contraceptive Use*, Categories 3 and 4 (Curtis et al., 2016).
- Clients whose medical condition has changed so that they might be using CHCs in the presence of relative or absolute contraindications as defined by the *U.S. Medical Eligibility Criteria for Contraceptive Use*, Categories 3 and 4 (Curtis et al., 2016).
- Clients with chronic health conditions that increase serum potassium or clients taking medications that increase serum potassium if considering use of a CHC containing drosperinone.
- Clients who are currently taking CHCs and demonstrate any of the following symptoms:
  - ACHES (abdominal pain, chest pain, headache, eye problems and severe leg pain)
  - unexplained vaginal/genital bleeding
  - jaundice
  - syncope
  - blood pressure >140/>90
  - history or current severe migraine headaches with aura
  - severe depression
  - severe allergic skin rash.
- Intravaginal/intragenital ring users with a history of Toxic Shock Syndrome (TSS). Rare cases of TSS have been reported by ring users though causation has not been determined.
- Clients reporting headaches that are new and/or worsening with the use of hormonal contraception (Curtis et al., 2016).
- Clients taking medications that might be affected by hormonal contraception.

Drug Interactions

The *U.S. Medical Eligibility Criteria for Contraceptive Use* identifies the following drugs and drug classes as Category 3 or 4 and could have some effect on CHC absorption (Curtis et al., 2016). RN(C)s must refer or consult with a physician or nurse practitioner for clients taking any of the following:

- Anticonvulsants: phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine, lamotrigine alone

  Note: *Lamotrigine/valproate combo does not interact with hormones (WHO, 2015).*

- Antimicrobials: Rifampicin or Rifabutin therapy

  Note: *With the exception of Rifampicin or Rifabutin therapy, antibiotic use does not affect hormonal contraceptive efficacy. Barrier methods should be used while on Rifampicin or Rifabutin therapy. Hormonal contraceptives should not be stopped. Antibiotics need to be taken for their full course. (Simons et al., 2017).*

- Fosamprenavir (antiretroviral) (WHO, 2015)

The following drugs may be impacted by CHC use. RN(C)s must refer or consult with a physician or nurse practitioner for clients taking any of the following (WHO, 2015):

- Clients taking theophylline, tricyclic antidepressants, diazepam or lithium, who may require dosage adjustments.
- Clients taking CHCs containing drospirenone. Drospirenone may increase potassium. Clients should be advised to inform their healthcare provider if they have kidney, liver, or adrenal disease as the use of Drospirenone-containing CHCs in the presence of these conditions could cause serious heart and/or health problems. Clients should also inform their healthcare provider if they are currently on daily, long-term medications for chronic conditions such as NSAIDs, potassium-sparing diuretics, potassium supplementation, ACE inhibitors, or angiotensin-II receptors antagonists, heparin, aldosterone antagonists, or strong CYP3A4 inhibitors.

PREGNANCY AND BREASTFEEDING/CHESTFEEDING

There is no known harm to the person, the course of the pregnancy, or the fetus if CHCs are inadvertently used during pregnancy (WHO, 2015). However, if a CHC is inadvertently initiated with a pregnant client or the client becomes pregnant during CHC use, the CHC should be discontinued immediately (WHO, 2015).

Postpartum

Initiation of CHC in the post-partum period is dependent on level of risk (Curtis et al., 2016). A summary is provided but a detailed breakdown can be reviewed in the most up-to-date *U.S. Selected Practice Recommendations for Contraceptive Use* (Centre for Disease Control and Prevention, 2016).

U.S. Medical Eligibility Criteria Category 4 (Curtis et al., 2016)

- Less than 21 days post-partum

U.S. Medical Eligibility Criteria Category 3 (Curtis et al., 2016)

- Breastfeeding/chestfeeding: 21 to < 30 Days
- Breastfeeding/chestfeeding: 30–42 days postpartum with other risk factors for VTE such as:
  - age ≥35 years
  - previous VTE
  - thrombophilia
  - immobility
  - transfusion at delivery
  - peripartum cardiomyopathy
  - BMI ≥30 kg/m2
  - postpartum haemorrhage

  - postcesarean delivery
  - preeclampsia
  - tobacco use (smoking)
- Non breastfeeding/chestfeeding: 21–42 days postpartum with other risk factors for VTE such as:
  - age ≥35 years
  - previous VTE
  - thrombophilia
  - immobility
  - transfusion at delivery
  - peripartum cardiomyopathy
  - BMI ≥30 kg/m2
  - postpartum hemorrhage
  - post cesarean delivery
  - preeclampsia
  - tobacco use (smoking)

Breastfeeding/Chestfeeding

Conflicting studies suggest theoretical concerns about the effects of CHCs on breast milk/human milk volume. Estrogen and progestin are both excreted in breast milk/human milk in small quantities, but are unlikely to have an effect on the baby (WHO, 2015).

PRECAUTIONS AND CONSIDERATIONS

In general, for all CHCs, the risk of VTE is highest in the first year of use and in first-time users (Black et al., 2017). The risk of VTE in CHC users remains significantly less than the risk of VTE in pregnancy and the post-partum period.

CHCs should not be withheld from clients with a family history of venous thromboembolism (VTE) unless they demonstrate symptoms of VTE. Family history of VTE in a first degree relative is a category 2. Some thrombophilia conditions that increase the risk for a deep vein thrombosis (DVP) or pulmonary embolism are heritable. Testing for underlying thrombophilias might be indicated for clients with a personal family history of VTE in a first degree relative with a history of spontaneous VTE (i.e.: not associated with pregnancy, cancer, airline travel, surgery, obesity, immobilization etc). In the absence of symptoms, routine laboratory screening for thrombophilia or other bleeding disorders is not recommended (Black et al., 2017). Additionally, screening of asymptomatic clients is not recommended.

Precautions and Considerations Specific to Oral CHCs (Black et al., 2017)

- Malabsorption related to chronic gastrointestinal inflammation and active diarrhea might cause ineffectiveness of any oral contraception.
- Repeated vomiting (e.g., bulimia) and/or severe diarrhea can decrease the absorption of the pill and might decrease its effectiveness. Vomiting within two hours of pill ingestion might require repeated doses.
- The effectiveness of oral CHCs might be slightly decreased among clients who are obese (BMI >30). However, no association has been found between pregnancy risk and body mass index (BMI). It is likely that even a small decrease in effectiveness in clients who are obese still confers high overall effectiveness.

Precautions and Considerations Specific to Transdermal CHCs (Black et al., 2017; Hatcher et al., 2018)

- The effectiveness of the patch might be slightly decreased among clients weighing greater than 90 kg or who are obese (BMI >30). However, no association has been found between pregnancy risk and body mass index (BMI). It is likely that even a small decrease in effectiveness in clients who are obese still confers overall effectiveness to be high and therefore should not be a reason to avoid this method.
- Clients with conditions that affect the skin, such as eczema, psoriasis, cuts, rash or sunburn, should not apply the patch to these areas.

Precautions and Considerations Specific to Intravaginal/Intragenital CHCs (Black et al., 2017)

- Clients who have significant medical constraints such as those listed below are not good candidates for the intravaginal/intragenital ring:
  - pelvic relaxation
  - vaginal/genital stenosis
  - utero-vaginal/utero-genital prolapse
  - physical constraints such as vaginal/genital obstruction
  - inability to reach their own genitalia
  - desire not to touch their genitalia due to previous trauma or gender dysphoria.
- Intravaginal/intragenital CHCs might not be suitable for clients who have conditions that make the vagina/genital area more susceptible to irritation or ulceration.
- Clients who have genital outbreaks of herpes simplex virus are able to use the intravaginal/intragenital contraceptive ring.
- Intravaginal/intragenital CHCs should not be used in conjunction with the diaphragm/cervical cap as it could dislodge this barrier.

ADVERSE EFFECTS

Side effects from CHCs are often mild and transient and can respond to a change in formulation (Black et al., 2017). Acknowledgment and management of side effects are crucial to successful continuation of CHCs.

A theoretical understanding of the different side effects implicated by hormones is helpful. The Society of Obstetricians and Gynecologists of Canada (SOGC) or the *U.S. Medical Eligibility Criteria Selected Practice Recommendations for Contraceptive Use* (Centre for Disease Control and Prevention, 2016) *and U.S. Medical Eligibility Criteria for Contraceptive Use* (Curtis et al., 2016) have resources for understanding side effects related to contraceptives that can be used as a resource for health care providers.

Common Possible Side Effects

Common side effects of CHCs include, but are not limited to (Hatcher et al., 2018):

- Absence of withdrawal bleed
- Appetite changes (can result in weight gain)
- Breast/chest tenderness
- Breakthrough bleeding/spotting
- Mild headaches without aura
- Nausea
- Mood changes
- Libido changes
- Skin changes

Warning and Precautions

Serious side effects from CHCs are rare (Hatcher et al., 2018). The following symptoms should be investigated immediately, referred to a physician or nurse practitioner, and might warrant discontinuation of CHCs:

- ACHES (abdominal pain, chest pain, headache, eye problems and severe leg pain)
- Moderate to severe depression
- Jaundice
- Unexplained vaginal/genital bleeding
- Syncope
- Blood pressure >140/>90
- Severe or worsening migraine headaches with or without aura
- Severe allergic reaction

CLIENT EDUCATION SPECIFIC TO CHC USE

Missed or Late CHC Doses

If available, advise the client to follow the product monograph, or advise the client to contact a health care provider or clinic. Some clinics choose to develop client hand-outs or resources specific to missed or late CHC doses. The Society of Obstetricians and Gynecologists of Canada (SOGC) or the *U.S. Medical Eligibility Criteria Selected Practice Recommendations for Contraceptive Use* (Centre for Disease Control and Prevention, 2016) have guidelines for missed hormonal contraceptives that can be used as a resource for health care providers.

Continuous Use, Extended Use, and Shortened Hormone Free Intervals (Black et al., 2017; Hatcher et al., 2018)

- When determining CHC method of use, the RN(C) should discuss continuous use, extended use, and shortened hormone-free intervals with the client.
- All oral, transdermal and vaginally/genitally administered CHCs can be used as continuous, extended use and/or with shortened hormone free intervals.
- Continuous use, extended use and shortened hormone-free intervals increase contraceptive efficacy and is associated with some benefits such as fewer overall missed pills.
- The rate of side effects and adverse events with continuous use regimes is similar to conventional CHC use.
- The length of the continuous use or extended use of CHC regimens should be administered according to the preference of the client.

Common Side Effects of Continuous and Extended Use (Hatcher et al., 2018)

The most common side effect of continuous and extended use of CHCs is irregular bleeding or spotting. This might result in higher discontinuation rates than 28-day CHC regimes or shortened hormone free interval regimes. It is important to counsel clients on how to manage these side effects and inform them that the unscheduled bleeding will decrease over time.

PRESCRIBING AND/OR DISPENSING

For prescribing and/or dispensing of CHCs, refer to the Contraceptive Management: Assessment DST.

The intravaginal/intragenital contraceptive ring is a cold chain medication. Once the cold chain has been broken, it is stable at room temperature for up to four months (Hatcher et al., 2018). An "insert by" expiry date, 4 months from time of cold chain breakage, should be clearly labelled on the outside of the ring package.

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APPENDIX 1: CHC SCREENING TOOL

This does not replace the most current practice recommendations. RN(C) should always check medical eligibility against the most current US Medical Eligibility Criteria.

Are there any relative or absolute contraindications for Combined Hormonal Contraceptive Use?		
Questions to assist in determining Medical Eligibility for CHC use:		
Have you ever been told you have breast cancer/chest cancer?	NO	YES
Have you ever had a stroke or problems with your heart?	NO	YES
Have you ever had a blood clot in your leg or lungs?	NO	YES
Have you ever been told you have a bleeding disorder?	NO	YES
Have you ever been told you have gall bladder disease, liver disease or jaundice?	NO	YES
Have you ever been told you have diabetes?	NO	YES
Have you ever been told you have lupus?	NO	YES
Have you ever been told you have high blood pressure or high cholesterol?	NO	YES
Have you ever had an organ transplant?	NO	YES
Do you have problems with severe diarrhea, poor absorption or other bowel disorders?	NO	YES
Do you get migraine headaches?	NO	YES
Are you planning any major surgery in the next 6 months?	NO	YES
Do you smoke cigarettes?	NO	YES
Have you been pregnant in the past 42 days?	NO	YES
Are you currently breastfeeding/chestfeeding?	NO	YES
Do you take any medications including natural remedies?	NO	YES
Do you take anti-retroviral medications?	NO	YES
Do you take medications for seizures?	NO	YES
Do you take medications for tuberculosis?	NO	YES

IF YES to any:
STOP - EXPLORE OR REFER

Client may not be a good candidate for CHC. Counsel about other contraceptive methods or consult/refer to Dr/NP if client is a MEC category 3 or 4.

IF YES to any:
STOP – EXPLORE

Further assessment required. Evaluate client condition. If client is MEC category 3 or 4 consult/refer to Dr/NP.