Oral hormonal contraception in special circumstances

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Background

Despite the general consensus that long-acting reversible contraceptives (LARCs) are the most appropriate choice of contraception for most women, there are special circumstances when the contraceptive and non-contraceptive needs of the patient are met by oral methods.

Objective

By using case histories, we seek to demonstrate the medical and practical complexities in managing contraceptive needs that may result in oral contraception being the most appropriate choice. The cases also illustrate the resources available to enable evidence-based management.

Discussion

Concurrent medical conditions and non-contraceptive benefits of oral contraceptive methods will see the continued use of these medications for a significant minority of women. A comprehensive knowledge of the rapidly developing evidence regarding medical eligibility and indications for usage is required. Reference to the already highly developed and easily accessible evidence bases ensures best practice for the women and families who seek advice.

Despite the increasing availability and acceptability of long-acting reversible contraceptives (LARCs), there will always be patients for whom oral contraception best addresses their contraceptive needs, while offering management of other concerns. It is important to tailor contraceptive advice accordingly, and maximise potential non-contraceptive benefits. Therefore, practitioners need to become agile at assessing indications and contraindications for various contraceptive preparations if a woman wishes to commence or continue with an oral method of contraception.

Medical eligibility criteria (MEC) were developed by the World Health Organization (WHO) and UK Faculty of Sexual and Reproductive Medicine (referred to as the UKMEC guidelines).[1,2] Both organisations use the same categorisation of advice and vary only slightly in those categorisations for specific conditions. Unless otherwise mentioned, this article adheres to the advice in the UKMEC guidelines (Box 1),[2] which were endorsed by Family Planning Alliance Australia.

It can seem daunting to negotiate the literature and guidelines when confronted with particular clinical situations. Therefore, this article uses the following case histories to provide illustrations of the potential complexity of the contraceptive consultation and the benefit of a comprehensive assessment of individual circumstances.

Case 1 – Elena

Elena, aged 38 years, requests a repeat script of her combined oral contraceptive pill (COCP). She has two children and regards her family as complete. Elena has a past history of postnatal depression (PND), which required antidepressant medication, now ceased, and describes cyclic mood disturbances as an adolescent. She used the levonorgestrel-secreting intrauterine-system between children, but started on the COCP after her second child, when she developed recurrent ovarian cysts, requiring laparoscopy for a torted

ovary. Elena has gained weight steadily since becoming pregnant with her first child. She finds it difficult to juggle paid employment, childcare responsibilities, and time to pay attention to diet and exercise. Elena mentions a maternal aunt who died of breast cancer in her 40s and wonders if she should 'have a break from the pill' again. She has never smoked. On examination, her weight is 90 kg, height is 167 cm, body mass index (BMI) is 32 kg/m^2, blood pressure, measured on two occasions, is 145/90 mmHg.

The COCP confers potential suppression of Elena's recurrent, benign ovarian cysts that have been problematic.[3,4] Further, her cyclic depressive symptoms and history of PND indicate another potential benefit of running the packets together to alleviate perimenstrual dysphoric symptoms. The third-generation drosiperone-containing COCP has been trialled against placebo and found to improve mood scores.[5] Other monophasic COCPs have not been trialled but represent a theoretical advantage by tri-cycling packets,[6] where the patient takes three packets sequentially without a pill-free interval. The 24/4 version of the drosiperone-containing COCP has a lower oestrogen component, which may confer benefits, including reducing cardiovascular risk and decreasing the pill-free interval.[7]

While the incidence of coexisting conditions increases with age, one needs to be mindful of the effect of age itself on COCP risk, with women aged ≥40 years being MEC2, and prescription generally not recommended in women aged >50 years.

Increased BMI is associated with an increased risk of venous thromboembolic events.[8] When considering initiating or continuing the COCP, Elena's BMI is categorised as MEC2 (benefits outweigh the risks) and, thus, the COCP may still be appropriate at this point. A BMI ≥35 kg/m^2 shifts Elena's risk to MEC3.[2] Therefore, in Elena's case, it is crucial to advise her regarding weight management. This finding together with her elevated blood pressure represent increasing cardiovascular risks. Again, weight management represents the key factor, as controlled hypertension (medicated) does not reduce the MEC3 category.[9]

A family history of breast cancer by itself does not increase Elena's personal risk and does not change her risk (MEC1). Should there be the presence of a known mutation, such as *BRCA1/2*, the risk with COCP increases (MEC3).[2]

There has been increased concern, in response to a recently published Danish study, regarding the relationship between hormonal contraception and depression.[10] This research considered women aged 15–34 years between 2000 and 2013. The study indicated that women were more likely to be diagnosed with depression or commenced on antidepressants for the first time if they were currently using or had recently used hormonal contraception. However, the data do not prove a causative relationship. There are many potential confounding factors. Further, previous observational studies in Europe and Australia found opposing results.[11,12]

Box 1. Definition of UKMEC categories for contraceptive use[2]

MEC1	A condition for which there is no restriction for the use of the contraceptive method Can use low-dose COCP*: women aged <40 years; post-partum ≥6 weeks and not breastfeeding; breastfeeding ≥6 months; superficial venous disease
MEC2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks Low-dose COCP* can be used in the following women, but careful follow-up may be required: aged ≥40 years; primarily breastfeeding <6 months; migraines; cardiovascular disease; dyslipidaemia; organ transplant; certain medications
MEC3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method Low-dose COCP* may be used, but expert clinical input may be required when other contraceptive methods are not available or acceptable: women aged ≥40 years; BMI ≥35 kg/m^2; adequately controlled hypertension; multiple risk factors for cardiovascular disease; history of ischaemic stroke and/or ischamic heart disease; complicated diabetes; acute hepatitis; certain medications
MEC4	A condition that represents an unacceptable health risk if the contraceptive method is used COCP should not be used immediately postpartum (<6 weeks) and breastfeeding; history of migraines with aura; atrial fibrillation; uncontrolled hypertension; impaired cardiac function; hormonal cancers; current/history of DVT; positive antiphospholipid antibodies; known thrombogenic mutations; smoking (≥15 cigarettes per day) and aged ≥35 years

**The recommendations in the UKMEC refer to low-dose combined oral contraception pill (COCP) containing <35 µg ethinylestradiol, combined with a progestogen (irrespective of their progestogen content)*
BMI, body mass index; COCP, combined oral contraception pill; DVT, deep venous thrombosis

We can reassure Elena that overall, COCP is of low risk for causing a return of her depressive symptoms. Further, such a concern needs to be weighed against the impact of an unwanted pregnancy on Elena's mental health and quality of life.

Case 2 – Nicole

Nicole, aged 20 years, sees you for contraceptive advice. She is in a new relationship and currently uses condoms for contraception and protection against sexually transmissible infections (STIs). Nicole's periods have been irregular and heavy since menarche at 12 years of age; her last menstrual period was approximately two months ago. Nicole also has increasing acne despite a daily antibiotic regime and waxing her top lip. She has gained almost 6 kg in the past year. Nicole has a family history of a cousin who had an unprovoked deep venous thrombosis in the past couple of years.

On examination, Nicole's height is 170 cm and weight is 85 kg, which gives her a BMI of 29 kg/m^2. She has no obvious signs of thyroid or other endocrine dysfunction, but she has widespread blackheads and evidence of facial hirsutism. A urine pregnancy test is negative.

It is important to make a pregnancy risk assessment and determine whether 'quick starting', a contraceptive method regardless of where Nicole is in her menstrual cycle, is appropriate.[13] This consultation is also an opportunity to perform an STI screen, ask about human papillomavirus vaccination status and discuss future cervical screening.

A useful exercise is for Nicole to prioritise her symptoms in terms of which she would like to see improved and to facilitate this through contraceptive choice. For example, if her acne and hirsutism are improved by a chosen COCP, her long-term adherence to this method is more likely. If, on the other hand, Nicole's fear of weight gain supersedes all other concerns, then reliance on a method least associated with appetite change or fluid retention is more appropriate. For example, a levonorgestre-secreting intrauterine system would also address her heavy menstrual bleeding.

Investigations of hormone status can be performed before commencing the COCP on the day of consultation. These include follicle-stimulating hormone (FSH), luteinising hormone (LH), prolactin, oestradiol, free androgen index (FAI), sex–hormone binding globulin (SHBG) and thyroid function status. In Nicole's case, it may be pertinent to also arrange a baseline pelvic ultrasound to document the endometrial thickness and assess the ovaries for possible polycystic appearance.

When counselling women regarding thrombotic risk and COCP, it is important to establish a baseline figure for comparison (Box 2). A family history of a second-degree relative with a venous thromboembolic event is not a contraindication to either the COCP or progestogen-only pill (POP). Nor does a negative thrombophilia screen change Nicole's original MEC1 based on her family history and merits initiating COCP if this becomes the final choice.[14] However, and most significantly, if she has a thrombogenic mutation, this is MEC2 for POP and MEC4 for oestrogen-containing methods. This latter is an absolute contraindication to prescribing COCP and a reason to change her method at the review appointment.

In a young woman whose baseline risk of a venous thromboembolic event is inherently low and who wishes treatment for acne and hirsutism, choosing a COCP containing drosiperone or cyproterone acetate is appropriate.[14,15] The POP requires greater adherence regarding the time it is taken, whereas the progesterone implant offers greater adherence. However, while both progesterone-only methods are MEC2, there is little evidence that either will offer improvement of her acne, hirsutism or indeed unscheduled bleeding.

Box 2. Comparative risks of venous thromboembolism in women of reproductive age[2]

Endpoint	Incidence (per 10,000 women)
Women not using any contraception	2
Women using COCPs containing levenogestrel or northisterone	5–7
Women using COCPs containing desogestrel, gestodene, drosiperone, nomegestrol, dienogest and the vaginal ring	6–12
Pregnancy	29
Post-partum	300–400

COCPs, combined oral contraceptive pills

Case continued – Nicole

Nicole's test results return a negative screen for thrombophilia, elevated FAI, decreased SHBG and slightly elevated LH to FSH ratio, indicative of polycystic ovary syndrome (PCOS). Ultrasonography confirms polycystic-appearing ovaries and an endometrial thickness within normal limits.

Many COCP varieties, not just those with antiandrogenic progestogens, will improve cycle control and, by increasing SHBG, will decrease circulating androgen and thereby improve acne.[16] Theoretically, progestogens containing drospirenone or cyproterone acetates may improve hirsutism, but require months to achieve this improvement. It is important to reassure Nicole that cosmetic interventions are not excluded and poor initial response to acne or hirsutism merit a dermatological referral. Finally, it is important to give lifestyle advice in the light of a PCOS diagnosis and recent weight gain.

Discussion regarding STI protection is the most important part of the consultation and must not be side tracked by the complexity of contraceptive concerns. Awareness of correct condom use and discussing this with a partner are crucial. Several applications and online sites maybe a useful guide (refer to 'Useful resources').

Case 3 – Teresa

Teresa is a South Korean woman, aged 26 years, who has been in Australia for three years and is newly sexually active. She currently uses condoms as contraception, but admits to episodes of unprotected sexual intercourse. Teresa has chronic hepatitis B (CHB), an infection she acquired from her mother perinatally, with no evidence of cirrhosis.

Teresa mentions that she is planning to travel overseas with her new boyfriend for six months through central and eastern Africa. Their travel plans include a trek up Mount Kilimanjaro (peak altitude at 5895 m) in Tanzania. She departs in four months.

Teresa takes no medication, and her blood pressure is 118/75 mmHg and BMI is 26 kg/m^2. She has no family or personal history of diabetes, migraine, cardiovascular disease or cancer.

Given Teresa's plans for long distance air travel, time to be spent at high altitude and her raised BMI, a LARC (eg IUD or implanon) was offered as the optimal contraceptive choice, but Teresa declined these.

In general, women need to consider if their current method of contraception is suitable for their intended travel, and what contraceptive services will be available in the countries they visit. They need to determine whether they can obtain replacement contraceptive pills, injections or vaginal rings in the event of theft, loss or need for renewal. The COCP and vaginal ring can provide Teresa with cycle control. The vaginal ring is less time-sensitive than the pill, so her scheduling for this method should not be affected by time zone differences of less than 24 hours.

Ask Teresa what bleeding pattern she is looking for, as many women prefer to avoid the inconvenience of having periods while travelling, and she may not be aware that this is an option. Menstrual bleeding can be avoided by continuous administration of the monophasic COCP (ie skipping the sugar tablets). The same can be achieved by skipping the hormone-free week for vaginal ring users. There are no additional safety concerns for women taking the monophasic COCP or vaginal ring continuously without hormone-free breaks for up to 12 months, but such use is off-licence.[14]

There is no restriction in initiating the COCP in women with CHB (MEC1) unless they have a flare (MEC3; refer to Box 3) or have acute hepatitis (MEC3), in which case the POP option may be used (MEC1). If Teresa commences the COCP, it must be taken every 24 hours.[14] When travelling out of the usual routine, it is easy to miss a pill. Refer to Box 4 for standard advice. If Teresa has significant vomiting or severe diarrhoea within two hours of taking her COCP, then the rule for missed pills should be applied.

If the time difference means that Teresa is potentially required to take the pill in the middle of the night, advise her to take it before she goes to bed instead of the following morning. Some women take a second watch that is set to the time at home and stick to their normal pill-taking routine. However, this may not always be convenient if she is travelling across a number of time zones. Irregular bleeding can occur because of hormonal changes due to time zone changes or disrupted routine, but this usually settles down. However, the irregular bleeding may represent pregnancy, which if likely, should be confirmed as soon as possible.

Women using the COCP or vaginal ring may have an increased risk of venous thromboembolic events during travel that involves long periods of immobility or if travelling to high altitudes.[18] Advise Teresa to reduce her periods of immobility and keep well hydrated for flights longer than three hours. Short-term travel at high altitudes poses no special problems. However, women spending more than a week at altitudes >4500 m should consider an alternative contraceptive method that does not contain oestrogen.[14]

Emphasise the importance of practising safe sex. Use of condoms is also advised in the context of her CHB. Her boyfriend needs to confirm his hepatitis B immunity, if this has not already been done. A supply of condoms when travelling is recommended. Emergency contraception may not be available in some African countries and Teresa should consider taking a supply.

Finally, Teresa will need a separate consultation to review her CHB status and discuss her other travel health needs – this can be combined with her pill review appointment.

Box 3. Key points – What is a chronic hepatitis B flare?[17]

- An acute hepatitis B flare is defined as an event with abrupt rise of alanine aminotransferase (ALT) levels to >5 times the upper limit of normal during chronic hepatitis B virus (HBV) infection.
- A flare may occur spontaneously, during or after antiviral therapy, and in the setting of immunosuppression and/or chemotherapy.
- The clinical spectrum of hepatitis B flares varies from asymptomatic to symptomatic, and typical overt acute hepatitis, even with hepatic decompensation or failure.

Box 4. Management of late or forgotten COCP*/vaginal ring – Seven-day rule[14]

A late pill is defined as being taken <24 hours late. Take the late hormone pill as soon as possible, then continue taking the pills as usual (two pills can be taken on the same day). No additional contraceptive required.
A missed pill is defined as being taken >24 hours late. The most recent pill should be taken, previously missed pills discarded, then continue taking the pills as usual (two pills can be taken on the same day). Additional contraceptive methods (eg condoms) or abstinence are required until seven consecutive active pills are taken.
Stopped use is defined as missing ≥4 consecutive pills, where the missed pill rule cannot apply. The woman should consider emergency contraception and restart the COCP.
Early cycle missed pill is defined as a pill missed in the first seven active pill days after the placebo. Emergency contraception should be considered if there was unprotected sexual intercourse in the past five days.
Late cycle missed pill is defined as missed pills in the past seven days of active pills before the next placebo pills. Skip the pill-free interval and continue the active pills without a break.

**These rules do not apply to the quadriphasic EV/dienogest COCP.*

Conclusion

The case histories described in this article are a few examples of a number of complex situations that may present during a

consultation for contraception advice. Through these cases, we have tried to highlight the need to undertake a risk assessment based on individual patient circumstances.

Useful resources

- UK Medical eligibility criteria for contraceptive use, www.fsrh.org/standards-and-guidance/external/ukmec-2016-digital-version
- Faculty of Sexual and Reproductive Healthcare of the Royal College of Obestricians and Gynaecologists (UK), Current clinical guidance on contraceptives, www.fsrh.org/standards-and-guidance/current-clinical-guidance
- World Health Organization Medical eligibility criteria (5th edn), www.who.int/reproductivehealth/publications/family_planning/MEC-5/en
- Family Planning New South Wales, Family Planning Victoria and True Relationships and Reproductive Health, Contraception: An Australian clinical practice handbook (4th edn)
- The National Campaign to Prevent Teen and Unplanned Pregnancy (US), Online birth control support network for women aged 18–29 years, www.bedsider.org/methods

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