14.21 Contraception for women with medical disease

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ESSENTIALS All women with underlying medical disorders should be given cor- rect advice regarding adequate contraception so that they can make informed choices regarding potential future pregnancies. There are several important factors to consider when deciding upon the most appropriate form of contraception to use. These include the risk of pregnancy for the woman, the effect of the contraceptive method on the medical disease, the failure rates associated with the contra- ceptive method, the consequences of an unplanned pregnancy, and the compliance and preferences of the individual woman. There are a small number of very high-risk conditions where pregnancy is not recommended due to high mortality rates, and the most reliable contraceptive methods should be recommended for these women. Introduction All women with underlying medical conditions should be given advice regarding adequate contraception so that informed choices regarding potential future pregnancies can be made. All special- ists involved in the care of women with medical disorders should have an understanding of the methods of contraception that are best suited for the needs of their patients and should be adequately trained in advising their patients regarding the most effective and safe contraception for them. It is the responsibility of the doctor seeing a woman for pre-conception or postpartum counselling to discuss the issue of contraception with her. Pre-conception counselling should optimize the woman’s medical condition(s) prior to pregnancy, ensure current drug treatment is compatible with pregnancy, and gain access to healthcare profes- sionals who have expertise in managing women with medical dis- eases in pregnancy. In the most recent Mothers and Babies: Reducing Risks through Audits and Confidential Enquiries (MBRRACE)-UK Reports, two-thirds of women died from indirect causes (not preg- nancy specific) and almost three-quarters of all women who died had co-existing medical complications. As in previous reports, car- diac disease remains the single largest cause of indirect maternal deaths. There was a lack of pre-pregnancy counselling for many of the women who died who had medical problems in pregnancy. It is important to disseminate accurate information

regarding contraception to all healthcare professionals responsible for looking after women with medical conditions. This is to avoid un- planned pregnancies in women receiving teratogenic medication, and in those for whom pregnancy carries an extremely high risk of maternal mortality or severe morbidity, as well as to avoid in- accurate advice to terminate pregnancy in women whose medical risk associated with pregnancy is low. For women who have more complex medical conditions, a multidisciplinary meeting involving specialist physicians and sexual and reproductive health specialists is advised. There are a small number of very high-risk conditions where pregnancy is not recommended due to a high risk of ma- ternal mortality or significant morbidity. These women should be counselled at length regarding the most reliable forms of contra- ception to use. There are several important factors to consider when deciding upon the most appropriate form of contraception in women with medical disorders. These include the risk of pregnancy for the woman, the effect of the contraceptive method on the medical dis- ease, the failure rates associated with the contraceptive method, the consequences of an unplanned pregnancy, and the compliance and preferences of the individual woman. In 2010, the World Health Organization (WHO) published the 4th edition of the Medical Eligibility Criteria for contraceptive use, which provides recommendations for the safety of various methods of contraception in women with a range of health conditions. There are four categories, ranging from category 1, where there is no re- striction for the use of the contraceptive method, to category 4 where the condition represents an unacceptable health risk if the contra- ceptive method is used (Table 14.21.1).
Contraceptive agents There is a variety of contraceptive agents available. They can be divided into hormonal and nonhormonal methods. The decision regarding contraception should be based on a risk–benefit analysis of the contraceptive method (Table 14.21.2). The individual patient’s risks of the contraceptive method adversely affecting the medical condition should be balanced against the risks of an unwanted pregnancy and its subsequent health implications for the woman. 14.21 Contraception for women
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 The most reliable contraceptive methods should be recommended for those women with the highest risk of mortality if pregnant. Hormonal methods Combined oestrogen-progesterone contraception These combinations of oestradiol (an oestrogen) and a progestogen (synthetic progesterone) inhibit ovulation and are very effective contraceptives. They include the combined oral contraceptive pill, the combined transdermal patch, and the combined vaginal ring. Relative and absolute contraindications for using combined hor- monal contraception are shown in Tables 14.21.3 and 14.21.4. The oestrogen component carries an increased thrombotic risk due to an increase in the circulating vitamin K-dependent clotting factors, an increase in plasminogen, a decrease in antithrombin, and an increase in platelet adhesion. Due to an increase in circulating volume, the risk of hypertension increases, and dyslipidaemia may worsen. Combined hormonal contraceptives should be avoided in women with a personal history of thromboembolic disease (WHO Class 4). Combined hormonal contraceptives containing levonorgestrel may carry a slightly lower risk of thromboembolic disease compared with other combined hormonal contraceptives. Combined hormonal contraceptives are associated with an in- creased risk of hypertension (risk ratio of 1.8), especially in women who have used them for more than five years. There is a very small absolute increase in the risk of ischaemic stroke in nonsmoking, normotensive women, and combined oral contraceptives are contraindicated in women with ischaemic heart disease, as there is Table 14.21.1 Meaning of category 1–4 recommendations in the WHO medical eligibility criteria (MEC) for contraceptive use Category

Meaning of category 1 A condition for which there is no restriction for the use of the contraceptive method 2 A condition where the advantages of using the method generally outweigh the theoretical or proven risks 3 A condition where the theoretical or proven risks usually outweigh the advantages of using the method 4 A condition which represents an unacceptable health risk if the contraceptive method is used Table 14.21.2 Points to be considered when deciding on the most appropriate contraceptive agent Points to be considered when deciding on the most appropriate contraceptive agent Efficacy Thrombotic risk (oestrogen-containing contraceptives) Arterial risks (oestrogen-containing contraceptives) Infection risk (e.g. insertion of an IUD) Vagal stimulation (e.g. insertion of an IUD/IUS, ESSURE®) Bleeding risks (e.g. with patients on anticoagulants) Interaction with concomitant drugs Effects of anaesthesia Ease of use/acceptability IUD, intrauterine device; IUS, intrauterine system. Table 14.21.3 Relative contraindications for using combined hormonal contraception (WHO Class 3) System Disease Arterial • Adequately controlled hypertension • Moderate hypertension untreated: SBP <160 mm Hg or DPB <95 mm Hg • Multiple risk factors for arterial disease Venous • First degree relative age <45 years with VTE • Immobility unrelated to surgery Endocrine • Diabetes mellitus with mild/moderate vascular disease/nephropathy/retinopathy/neuropathy Breast • Not breastfeeding <3 weeks postpartum • Fully breastfeeding ≥6 weeks to 6 months postpartum • Breast cancer >5 years ago without recurrence • Carriers of known gene mutations associated with breast cancer (e.g. BRCA1 and BRCA2) Metabolic • Some known hyperlipidaemias • Obesity 35–39 kg/m2 BMI Neurological • Previous migraine with aura at any age • Migraine with aura ≤35 years (continuation of contraceptive) • Migraine without aura ≥35 years (initiation of contraceptive) Liver • Current or medically treated gallbladder disease • Previous cholestasis due to combined oral contraceptives • Obstetric cholestasis Drugs • Liver enzyme inducers • Ritonavir-boosted protease inhibitors • Lamotrigine • Smoking <15 cigarettes/day and age ≥35 years • Stopped smoking <1 year ago BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; VTE, venous thromboembolism.

 a dose-related increased risk of myocardial infarction (odds ratio of 2.5). This risk increases almost 10-fold in women who are hyperten- sive, who smoke, or who have hyperlipidaemia. Due to the throm- botic risk, combined oral contraceptives are contraindicated in women with pulmonary hypertension. They should also be avoided in women with uncontrolled hypertension. Oestrogens and progestogens are metabolized by the liver and their use may adversely affect women who have abnormal liver func- tion. They also interact with warfarin metabolism so more frequent monitoring of the international normalized ratio is necessary when initiating treatment and adjustment of dose. It is also important to remember that liver enzyme inducers (Table 14.21.5) may result in reduced contraceptive efficacy of combined hormonal contra- ceptives. If combined hormonal contraceptives are used by women taking liver enzyme inducers, then the preparation should contain at least 50 µg of ethinyl oestradiol and barrier contraception should be used for up to four weeks following discontinuation of the liver enzyme inducer. Progestogen-only contraceptives Progestogens cause no significant changes in blood pressure, throm- botic risk, or lipid profile and are therefore suitable for most women with medical disorders where oestrogens are contraindicated, such as in cardiac disease or women at significant risk of thromboses. However, progestogen-only oral contraceptives have a higher failure rate than combined hormonal contraceptives. The contraceptive ef- fect relies on strict patient compliance, as etynodiol, norethisterone, and levonorgestrel must be taken within the same three-hour window each day in order to maintain contraceptive protection. Unlike other

progestogen-only oral contraceptives, desogestrel in- hibits ovulation, and the missed pill window is extended to 12 hours. Desogestrel (e.g. Cerazette®) may therefore benefit women who are suitable for progestogen-only oral contraceptives but have difficulty with compliance. Relative contraindications for using progestogen- only methods of contraception are shown in Table 14.21.6. Women with pulmonary arterial hypertension receiving bosentan need an increased dose of desogestrel, as bosentan induces the cyto- chrome P450 enzymes CYP2C9 and CYP3A4. They should also be advised to use a supplementary form of contraception, like condoms, as the risks associated with contraceptive failure in women with pul- monary hypertension are extremely serious. Progestogen-only oral contraceptives are a suitable form of contraception for women on long-term anticoagulation therapy, for example, those with metallic prosthetic cardiac valves. It is contraindicated in women with cur- rent breast cancer. Table 14.21.4 Absolute contraindications for using combined hormonal contraception (WHO Class 4) System Disease Arterial • Severe hypertension untreated: SBP ≥160 mm Hg or DPB ≥95 mm Hg • Hypertension with vascular disease (e.g. coronary heart disease, peripheral vascular disease, hypertensive retinopathy, transient ischaemic attacks) • Ischaemic heart disease • Cerebrovascular accident • Complicated valvular and congenital heart disease (e.g. with pulmonary hypertension, atrial fibrillation, history of bacterial endocarditis) • Multiple risk factors for cardiovascular disease (e.g. age, smoking, diabetes mellitus, hypertension, hyperlipidaemia) Venous • Thrombosis (deep vein thrombosis, pulmonary embolism, or cerebral venous thrombosis) • Major surgery with prolonged immobilization • Known thrombophilia Endocrine • Diabetes mellitus >20 years • Diabetes mellitus with severe vascular disease or severe nephropathy, retinopathy, or neuropathy Breast • Breastfeeding <6 weeks post-partum • Current breast cancer Metabolic • Obesity ≥40 kg/m2 BMI Neurological • Migraine with aura • Migraine without aura and age ≥35 years (continuation of contraceptive) Liver • Active viral hepatitis • Severe (decompensated) cirrhosis • Benign or malignant liver tumours Connective Tissue • Systemic lupus erythematosus with anticardiolipin antibodies/lupus anticoagulant Drugs • Smoking ≥15 cigarettes/day and age ≥35 years Table 14.21.5 Examples of enzyme inducers that can result in reduced contraceptive efficacy of combined hormonal contraceptives Liver enzyme inducers Rifampicin Rifabutin Griseofulvin Phenytoin Carbamazepine Oxcarbamazepine Primadone Barbiturates St John’s Wort

 The newer long-acting progestogen-only oral contraceptives (levonorgestrel-releasing intrauterine system, LNG-IUS; Mirena®, and the progesterone implant, Nexplanon®) are the most effica- cious contraceptives available, providing contraceptive protection comparable to that of sterilization. The LNG-IUS system requires replacement every five years and works by releasing 20 µg of levo- norgestrel directly into the uterus, causing endometrial shedding and subsequently light periods. Most women with a LNG-IUS be- come oligoamenorrhoeic, which is a major advantage in women receiving long-term anticoagulation therapy who may suffer from menorrhagia, as well as those women with cyanotic heart disease who would not tolerate anaemia from heavy periods. Women with pulmonary arterial hypertension or a Fontan circulation may not tolerate a bradycardiac response to cervical instrumentation. So in these women, LNG-IUS insertion should be performed in a hos- pital setting with anaesthetic support. Women should be screened for sexually transmitted infections or empirically covered with anti- biotics, and those at risk of infective endocarditis should be given appropriate antibiotic prophylaxis for insertion. Women with puer- peral sepsis, following a septic abortion or with current pelvic in- flammatory disease should not have an intrauterine device inserted. In women with ischaemic heart disease and hyperlipidaemia, the LNG-IUS provides the

safest lipid profile, as levels of high-density lipoprotein are increased. Depot medroxyprogesterone acetate (DMPA) is an effective contraceptive injection that has no cardiac contraindications. Good compliance with 12-weekly injections is important for contraceptive effectiveness. However, deep intramuscular injections may cause significant haematomas in those receiving anticoagulation therapy. Amenorrhoea is a common side effect and may be an advantage in women with cyanotic heart disease, many of whom suffer from men- orrhagia. In women with ischaemic heart disease there is a small the- oretical concern that DMPA may cause a moderately unfavourable alteration in lipid metabolism. In women taking enzyme-inducing drugs such as bosentan, or in women with significantly raised BMI, additional supplemental progestogen may be required. Fertility re- turns to normal within six months of cessation of treatment. Nexplanon® is a radio-opaque etonogestrel-releasing implant. It has replaced Implanon® and has no cardiac contraindications. Nexplanon® is as effective as sterilization and produces steadier blood levels, and fewer side effects, than injectable contraceptives. There is much less risk of haematoma formation, as the implant is subdermal and only needs replacing every three years. The inter- national normalized ratio should be checked prior to insertion in women taking warfarin. The efficacy of contraceptive implants is affected by bosentan, so an additional method of contraception should be used in order to provide reliable contraception for women with pulmonary hypertension. Copper intrauterine contraceptive device The copper-releasing intrauterine device (IUD) works by inhibiting fertilization, as well as implantation, without the need for exogenous hormones. As with the LNG-IUS, it is recommended that prophy- lactic antibiotics be administered at the time of insertion of the intrauterine device, if the woman has not been screened for sexually transmitted infections. In all women, the risks of intrauterine contraception include uterine perforation, infection, and displacement of the IUD. It should, therefore, be avoided in women with previous infective endocarditis, and used with caution in the presence of complicated valvular disease or in those who are anticoagulated. IUDs are not re- commended in immunosuppressed women, for example, those who have undergone heart or kidney transplantation, due to the risk of infection, and it should be avoided in cases of puerperal sepsis. Emergency hormonal contraception The first choice of oral emergency hormonal contraception is 1.5 mg of levonorgestrel, taken as a single dose. This should ideally be taken within 12 hours of intercourse but no later than 72 hours for best ef- fect. An alternative form of emergency contraception, if the woman exceeds the 72-hour window, is 30 mg of ulipristal acetate, a selective progesterone receptor modulator, which is licensed for administration up to 120 hours after intercourse. Alternatively, a copper IUD may be inserted up to 120 hours after intercourse. Insertion, how- ever, carries risks of vagal reaction and infection, as previously dis- cussed. In women who are treated with warfarin, the international normalized ratio should also be monitored after emergency oral contraception, as this can be affected. Table 14.21.6 Relative contraindications for using progestogen-only methods of contraception (WHO Class 3): All methods unless specified System Disease Arterial • Hypertension with vascular disease (injectables) • Multiple risk factors for cardiovascular disease (e.g. age, smoking, diabetes mellitus, hypertension, hyperlipidaemia) (injectables) • Ischaemic heart disease (injectables; POP/IMP initiation or continuation of contraceptive) • Cerebrovascular accident (injectables; POP/IMP initiation or continuation of contraceptive) Endocrine • Diabetes mellitus >20 years (injectables) • Diabetes mellitus with vascular disease (i.e. nephropathy, retinopathy, or neuropathy, injectables) Breast • Breastfeeding <6 weeks postpartum • Breast cancer >5 years ago without recurrence Neurological • Migraine with aura (all methods: continuation of contraceptive) Liver • Active viral hepatitis • Severe (decompensated) liver cirrhosis • Tumours: benign/malignant liver tumours Drugs • Liver enzyme inducers (POP/IMP) IMP, implant; POP, progesterone-only pill.

14.21 Contraception for women with medical diseases 2715 Nonhormonal methods Female sterilization Female sterilization carries a 10-year failure rate of 2–3/1000 when performed laparoscopically with Filshie clips, and a lifetime failure rate of 5/1000. If the sterilization is performed at the same time as a caesarean section, the 10-year failure rate is higher (approximately 7.5/1000). Laparoscopic sterilization is usually performed under general anaesthesia. A carbon dioxide (CO_2) pneumoperitoneum is created, which reduces venous return and has the potential for the CO_2 to be systemically absorbed. This can result in paradoxical emboli in women with right to left shunts. Laparoscopic sterilization can usually be performed without instrumentation of the cervix, but if instrumentation is essential in order to manipulate the uterus to gain better access to the fallopian tubes, it can result in a vasovagal response, which may not be tolerated in those with pulmonary vas- cular disease. ESSURE® is a new sterilization method in which intratubal stents are hysteroscopically inserted into the proximal section of the fal- lopian tubes using oral analgesia or light sedation. Tubal occlusion occurs by three months due to mechanical obstruction and inflam- mation causing fibrosis. The incidence of vasovagal attacks from the insertion of the hysteroscope is 1.85%. Male sterilization Vasectomy is more efficacious than female sterilization and has the added benefit of involving no risk to the woman. It is performed under local anaesthetic but should be a very considered choice if it is to be used as contraception in the partner of a woman with severe medical disease whose lifespan may be significantly reduced, as he may wish to father children in the future with a new partner. Barrier methods Neither male nor female condoms are very effective methods for prevention of pregnancy but should be used to prevent sexually transmitted infections. They should be used with a more reliable contraceptive method. Termination of pregnancy If a woman with a high-risk medical condition becomes pregnant and the continuation of the pregnancy carries with it a high risk of maternal mortality or severe morbidity, termination of pregnancy should be discussed with the woman and facilities made available. Medical termination of pregnancy can be performed at any gesta- tion and is usually carried out by administering oral mifepristone, followed two days later by a prostaglandin, misoprostol. Surgical termination of pregnancy is performed by suction, or dilatation and evacuation at more advanced gestations up to 24 weeks. Cervical priming with prostaglandins may be required. Specific medical conditions Hypertension Combined oral contraceptives with low-dose oestrogen formu- lations increase ambulatory blood pressure in normotensive and mildly hypertensive women by 6–8 mm Hg compared with users of the copper IUD. The risk is highest among women who have used combined oral contraceptives for six or more years and the risk decreases shortly after the combined oral contraceptive has been stopped. Progestogen-only oral contraceptives do not in- crease blood pressure and so are considered safe contraceptives in hypertensive women. Arterial disease Combined hormonal contraceptives should not be used in women with a history of ischaemic heart disease or stroke. The risk of stroke and myocardial infarction are thought to be related to the dose of oestrogen, with those taking the lower dose oestrogen preparation at lower risk. Users of low-dose combined oral contraceptives with second-generation progestogens have a higher risk of stroke than those using third-generation progestogens. Smoking and hyperten- sion further increases the risk of stroke and myocardial infarction in combined oral contraceptive users by up to 10-fold. There is no increased risk of stroke or myocardial infarction in users of the progestogen-only oral contraceptives. However, in- jectable and implantable progestogens should be used with cau- tion in those with a history of ischaemic heart disease or stroke, as studies have shown a reduction in high-density lipoprotein and an increase in low-density lipoprotein in those on DMPA, and a reduction in high-density lipoprotein and low-density lipopro- tein and an increase in triglyceride levels in those women using

Nexplanon®. LNG-IUS has been shown to have a better lipid profile with an increase in high-density lipoprotein levels, so if a woman using Nexplanon®, DMPA or the progesterone-only pill develops ischaemic heart disease or a stroke, she should consider changing to LNG-IUS or the copper IUD. Thrombosis There is a three to fivefold increased risk of venous thrombo- embolism in women taking oestrogen-containing contraceptives compared with nonusers, as oestrogen is pro-thrombotic due to increases in the hepatic production of some clotting factors (Table 14.21.7). However, pregnancy itself carries a 12-fold increased risk of venous thromboembolism. Desogestrel and gestodene, which are third-generation progestogens, are twice as thrombotic as second-generation progestogens, and the overall risk increases with age and obesity. The WHO recommends that combined hormonal contraceptives should not be used in women who have had an idiopathic venous thromboembolism or a venous thromboembolism associated with pregnancy or previous use. Women with known thrombophilias should not use combined hormonal contraceptives as they have an Table 14.21.7 Risks of venothrombolic events with combined oral contraceptives and pregnancy Category Risk of VTE per 100 000 women Healthy nonpregnant, nonusers of COC 5 Second-generation COC 15 Third-generation COC 25 Pregnancy 60 COC, combined oral contraceptive; VTE, venous thromboembolism.

Section 14 Medical disorders in pregnancy 2716 increased risk of venous thromboembolism, which is further in- creased by 2–20-fold if they start combined oral contraceptives. The copper IUD and progestogen-only oral contraceptives are thought to be safer than the combined hormonal contraceptives for women at risk of venous thromboembolism, although caution should be used as there is an increased risk of haematoma formation with injectables or Nexplanon®, and with bleeding at the time of in- sertion of LNG-IUS in women on anticoagulants. Pulmonary arterial hypertension Pulmonary arterial hypertension is associated with maternal mor- tality rates of up to 25%. Nexplanon® is the most suitable method of contraception in women with pulmonary hypertension as it is highly efficacious and avoids the complications of injectables and IUDs. Injectables are unsuitable, as most patients with pulmonary arterial hypertension are anticoagulated with warfarin. IUD inser- tion results in a vasovagal episode in at least 1.2% of women due to cervical dilatation, and the incidence is greater with the LNG-IUS insertion than with copper IUDs due to the larger width of the LNG-IUS. Bradycardias are poorly tolerated in pulmonary arterial hypertension and can lead to circulatory collapse. If IUD use is considered necessary, it should be inserted in hospital with an an- aesthetist present and atropine at hand. Combined hormonal contraceptives are contraindicated due to their thrombotic risk. As previously mentioned, female sterilization may be performed without instrumenting the uterus, but vasectomy is not usually recommended as the male partner will usually outlive the woman. Migraine The combined oral contraceptive increases the risk of stroke in women with migraine by 2–4-fold. Aura occurs before a headache and specifically relates to focal symptoms indicating ischaemia and includes unilateral sensory or motor symptoms and speech disturb- ance. Aura is also considered to increase the risk of stroke, and the mechanism is thought to be due to a reduction in cerebral blood flow to certain areas and increased platelet activity. The combined oral contraceptive is WHO Class 3 in women with migraine without aura, and WHO Class 4 in those with aura. Progestogen-only oral contraceptives have been given WHO Class 2 and the copper IUD is Class 1 for women with migraine with aura. Diabetes Women with diabetes should have their glucose control optimized around the time of conception, as the risk of major congenital ab- normalities is directly related to glycaemic control, so effective contraception for women with diabetes is especially important. Women with poorly controlled diabetes are also at risk of miscar- riage, macrosomia, pre-

eclampsia, and intrauterine growth restric- tion and intrauterine fetal death. The copper IUD is recommended (WHO Category 1) for women with diabetes, although as previously mentioned, there is a risk of infection with this method. Reports that have suggested that carbohydrate and lipid metab- olism are affected by hormonal contraception, especially glucose metabolism with high-dose combined oral contraceptives, but the studies involved are small. There are no long-term studies on the progression of vascular complications in women with diabetes who are on hormonal contraceptives, but the threat of arterial events limits the use of combined hormonal contraceptives to nonsmokers under the age of 35 years who are normotensive, without any vas- cular complications. Epilepsy Epilepsy affects approximately 0.5–1% of women of childbearing age and is the commonest neurological disorder seen in preg- nancy. Women with epilepsy should ideally be referred to a neur- ologist before getting pregnant. A re-evaluation of the need for and choice of antiepileptic drug treatment, including whether the diagnosis is correct and whether the epilepsy has spontaneously remitted, is important. The aim is to treat with one antiepileptic drug at the lowest effective dose. If one antiepileptic drug is re- placed with another felt to be more suitable for pregnancy, this may involve a period of overlap of two antiepileptic drugs, which increases the risk of congenital malformations. Contraception counselling is vital to avoid unplanned pregnancy in women taking antiepileptic drugs. The enzyme-inducing antiepileptic drugs, which include phenytoin, carbamazepine, phenobarbital, and topiramate, can accelerate the metabolism of oral steroids, and so high-dose oestrogen preparations may be needed to suppress ovulation. Lamotrigine is not an enzyme inducer, but its clearance may be accelerated when used with combined hormonal contraceptives which should be used with caution in women taking lamotrigine (WHO Class 3). As mentioned earlier, enzyme-inducing antiepileptic drugs decrease serum concentrations of both ethinyl oestradiol and progestogens. Because progesterone-only pills generally con- tain lower doses of progestin than doses found in combined oral contraceptives, there is a potentially high failure rate when taken in combination with enzyme-inducing antiepileptic drugs. As a result, progesterone-only pills should be prescribed with cau- tion (WHO Category 3). DMPA is WHO Category 1 for women using antiepileptic drugs. Contraceptive failure has been reported with the implant in women taking enzyme-inducing antiepileptic drugs. In contrast to combined oral contraceptives, progestogen- only oral contraceptives do not lower serum lamotrigine levels, so in women taking lamotrigine, progesterone-only pills, DMPA, and implants are WHO Category 1. Both the LNG-IUS and copper IUD can be used without restriction in women with epilepsy, and both enzyme-inducing antiepileptic drug and lamotrigine users can use them without restriction (WHO Category 1). Liver disease Women with a history of obstetric cholestasis or previous cholestasis while using combined hormonal contraceptives may develop cholestasis with subsequent use. This is also possible with progestogen-only oral contraceptive use, hence if hormonal contraception is used the patient should be monitored carefully for pruritus and abnormal liver function tests. Oestrogens and progestogens are metabolized by the liver, and their use may ad- versely affect those with active viral hepatitis, severe cirrhosis, and liver tumours where liver function is compromised. Combined hormonal contraceptive use is regarded as WHO Category 4 in these patients, whereas progestogen-only oral contraceptive use is

 graded WHO Category 3. The copper IUD can be safely used in women with liver disease. Sickle cell disease Advice regarding combined hormonal contraceptive use in women with homozygous sickle cell disease remains uncertain, with theor- etical concerns of promoting thromboses. DMPA reduces the in- cidence of painful crises in women with sickle cell disease, which makes it an attractive option for these women. Systemic

lupus erythematosus Combined hormonal contraceptives should be avoided in those with any evidence of vascular disease, lupus nephritis, or anti phospholipid antibodies, due to an increased risk of increased dis- ease activity and thrombosis. Progestogen-only oral contraceptives and the copper IUD are suitable and effective contraceptives in women with varying lupus disease severity.

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