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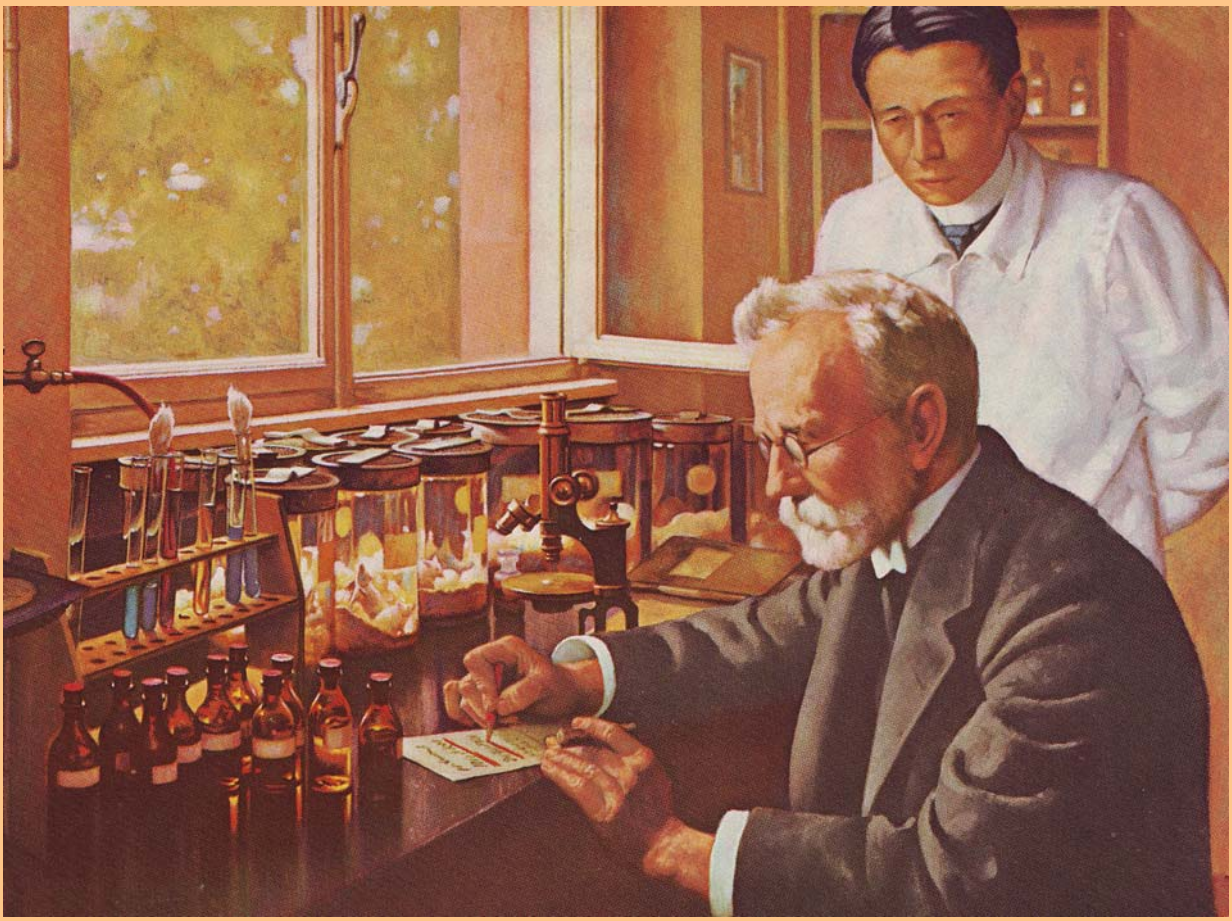

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The Sri Lanka Prescriber

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Cover picture

EHRLICH: CHEMOTHERAPY IS LAUNCHED

In a crowded laboratory at Frankfurt's Institute of Experimental Therapy, German research scientist Paul Ehrlich (1854-1915) habitually scrawled work orders to associates with stubby colored pencils on ''blocks'' of note paper. Dr. Ehrlich and his Japanese assistant, Dr. Sahachiro Hata, announced Salvarsan (606) to the world in 1910 as a ''chemical bullet'' for treatment of syphilis. Dr. Ehrlich's success with chemical synthesis gave impetus to a new medical science, chemotherapy. Though his greatest achievements were in this field, Dr. Ehrlich contributed to many branches of medicine and shared in a 1908 Nobel Prize for his work on immunology.

 Robert A. Thom, Artist

Safe use of oral cytotoxic medicines

Summary

The oral route is increasingly used to administer cytotoxic therapy for cancer and non-cancer conditions.

Oral cytotoxic therapy carries the same risk of medication errors as parenteral therapy.

It is essential that health professionals involved in providing oral cytotoxic therapies understand how they are used, what adverse effects can occur and how to minimize medication errors.

Key words: capecitabine, methotrexate

*(Aust Prescr 2013; **36**: 9-12)*

Introduction

Oral administration of cytotoxic therapy has increased over the past decade as newer drugs and formulations have become available (see Table). Cytotoxic chemotherapy is not restricted to cancer. Conditions including rheumatoid arthritis, psoriasis and other autoimmune diseases may be managed using oral medicines such as methotrexate.

The pros and cons of oral cytotoxic therapy

The oral route offers many advantages over the parenteral route of administration. Medicines can be administered in the community, without the need for venous access, and fewer visits to the hospital are needed.

While self-administration at home is convenient for both patients and carers, it can present a risk for the patient. Adverse effects can go undetected unless appropriate steps are in place to monitor the patient. Cytotoxic chemotherapy has a narrow therapeutic index and a small increase in dose can result in toxic effects, while under-dosing can lead to failure of therapy. Serious toxicities and fatal outcomes have occurred as a result of incorrect prescribing and dispensing as well as patient misinterpretation of dosing instructions.[1-6]

Responsibilities of the healthcare team

The safe delivery of oral cytotoxic therapy requires a multidisciplinary approach. Patients may be managed under shared-care arrangements between hospital specialists, general practitioners and community pharmacies.

All health professionals involved should:

- have appropriate training and skills in the use of cytotoxic chemotherapy and cancer care, when therapy is being used in this context[7]
- seek advice from a practitioner experienced in cytotoxic chemotherapy when required
- follow the principles of safe medication practices for oral cytotoxic medicines.

All patients should have a treatment plan. This is completed by the specialist who initiates the treatment[7] and should be given to the patient and all the healthcare professionals involved in their treatment. It is important that the patient has the plan with them if they see a different doctor, for instance in an emergency.

For the treatment plan to be useful, it should be explicit about:

- the patient's diagnosis
- the name of the chemotherapy protocol or specific cytotoxic medicine
- the expected number of cycles and the intended duration of treatment
- other adjuvant or concurrent treatments the patient is receiving (for example radiation therapy or surgery for cancer patients)
- expected adverse effects and their management.

Prescribing

Prescriptions for oral cytotoxic therapy should be clear and unambiguous. The term 'as directed' must not be used regardless of how long the patient has been on the therapy.

Table **Oral cytotoxic medicines**

Drug class	Drugs
Alkylating agents	busulfan, chlorambucil, cyclophosphamide*, lomustine, melphalan, procarbazine, temozolomide
Anthracyclines	idarubicin
Antimetabolites	capecitabine, fludarabine, hydroxyurea*, mercaptopurine*, methotrexate*, thioguanine
Podophyllotoxins	etoposide
Vinca alkaloids	vinorelbine

* currently used for both cancer and non-cancer indications

Prescriptions should specify:

- the generic drug name, number of tablets to be taken[7] and frequency and duration of therapy (written in full)
- whether the medicine is given on a cyclical or continuous basis. For example, capecitabine is frequently administered for 14 days of a 21-day cycle while temozolomide may be administered for 5 days of a 28-day cycle. The start and stop dates for a cycle should be clear.
- the day on which tablets should be taken. For example, methotrexate is most commonly given as a once-weekly dose (Box).[8] Fatal errors have occurred when methotrexate has been prescribed to be taken daily or when the incorrect strength of tablets has been prescribed.[9]

Wherever possible the quantity prescribed should be the quantity needed for one cycle (cancer chemotherapy) or one month (for example methotrexate for rheumatoid arthritis). Preferably, repeat prescriptions should not be issued as doses may change according to adverse effects and therapeutic response. If a repeat prescription is issued within the Pharmaceutical Benefits Scheme regulations, the patient should be directed to destroy any repeats or return them to the prescriber if treatment is changed or stopped.

Box **Safe prescribing of weekly methotrexate**[8]

Provide the patient with verbal and written information on the intended schedule of therapy including the dose as a quantity of tablets and the frequency of dosing

Ensure handwritten prescriptions are complete and legible and include in full the form, strength, dose and directions

Nominate on the prescription the day on which the dose should be taken

Do not write 'as directed' on the prescription

Consider limiting the prescribed quantity of methotrexate to four weeks

Do not override warnings and flags for methotrexate in prescribing software

Keep the strength of tablet supplied to the patient consistent to avoid confusion for the patient over the number of tablets they need to take

Be aware of signs of methotrexate toxicity or intolerance, for example dry persistent cough, vomiting and diarrhoea

Patients should be advised to contact their doctor or pharmacist straight away if a dose is missed, or they develop an infection such as gastroenteritis or fever

If a patient is admitted to hospital, strike out the six days of the week when methotrexate is NOT required in the administration section of the inpatient medication chart

Patients should always be advised on the action to take should they experience an adverse event – for example severe diarrhoea with capecitabine requires immediate cessation of therapy. Patients should be given the name of an accessible healthcare contact they can speak to regarding any concerns.

Dispensing and supplying oral cytotoxic treatment

The dispensing of oral cytotoxic therapy includes verification of the prescription for the patient and their

condition, and appropriate supply in a safe and timely manner.[7] For cancer chemotherapy the pharmacist should have access to the treatment plan, the chemotherapy protocol and relevant patient parameters including height and weight and recent laboratory results.[10] The pharmacist should ensure that the relevant supportive medicine has been prescribed or is available to the patient.

Interactions between chemotherapy, other prescribed drugs, and over-the-counter and complementary medicines can cause changes in the efficacy and safety of oral chemotherapy.[11] For example, analgesic doses of aspirin and non-steroidal anti-inflammatory drugs can increase the toxicity of methotrexate when they are used with cancer therapy. Low-dose aspirin can be used with weekly methotrexate. The risk associated with lower doses of methotrexate used in rheumatoid arthritis therapy is much less.

Conversely cytotoxic chemotherapy can alter the effectiveness of other drugs. For example, capecitabine significantly reduces the metabolism of warfarin, increasing its anticoagulant effect. A complete medication history should be taken from the patient or carer before dispensing a prescription and potential interactions should be discussed. If a dose administration aid (for example a Websterpak) is required by the patient, then oral cytotoxics must be packed separately from the patient's non cytotoxic medicines.

Medicine labelling

The labelling of oral cytotoxic therapy should clearly state the dose and the number of tablets to be taken. The label for weekly dosing for medicines such as methotrexate and vinorelbine should include the term 'once a week' and specify the day the dose should be taken. Cytotoxic chemotherapy can be carcinogenic, mutagenic and teratogenic. A warning sticker should be placed on all containers of cytotoxic chemotherapy tablets and capsules, in accordance with local health and safety policy. An adhesive purple sticker with the wording 'cytotoxic, handle with care' is recommended. A warning label must be placed on administration aid packs that identify the contents as cytotoxic. Oral cytotoxic tablets and capsules should not be broken or crushed as this can increase the risk of exposure and alter the bioavailability of the medicine.

Information for the patient

Patient information is paramount to support the safe use of oral cytotoxic therapy. Patients should be given verbal and written information that includes dose instructions (when the medicine should be taken and if it is required to be taken before or after food), adverse effects and safe storage instructions.[7,12] Some oral cytotoxic medicines need to be stored securely in a refrigerator, for example chlorambucil and melphalan.

Patients should be advised that oral cytotoxic medicine should only be taken out of the dispensed packaging immediately before a dose. To minimize exposure of carers and family members to cytotoxic medicines, patients should be advised that self administration is preferable. If administration by a carer is required then disposable gloves should be worn. Unused tablets must be returned to the local pharmacy or original supplier and not disposed of at home.

The intermittent, cyclical treatment that is characteristic of many cancer chemotherapy protocols is difficult for some patients to understand and they may misinterpret instructions. Medication guides, patient calendars and dose administration aids are often useful to help patients follow complex dose regimens, particularly those on multiple medicines. Adherence to oral therapy is important to maximize the benefits and reduce the risks of treatment. This should be discussed with the patient.

If appropriate, Consumer Medicine Information leaflets should be given to patients, however the context in which cytotoxic chemotherapy is used often limits their suitability. Patient information leaflets on many of the commonly used cancer chemotherapy protocols can be found on the eviQ Cancer Treatments Online website.[13] This website also provides information about how to safely take oral chemotherapy treatments at home.* The Australian Rheumatology Association provides patient information on drugs such as methotrexate and cyclophosphamide.[8]

(*www.eviq.org.au/Protocol/tabid/66/categoryid/449/id/492/Patient+Information++Oral+Chemotherapy.aspx)

Patients should be advised of the importance of notifying dentists, doctors and other healthcare, professionals who may be involved in their care about their cytotoxic therapy.

Identifying and managing adverse effects

Cytotoxic chemotherapy causes many adverse effects such as nausea, vomiting, bone marrow suppression, stomatitis, diarrhoea, hand-foot syndrome, peripheral and central neurotoxicity, renal and liver dysfunction and hair loss. The effects require careful monitoring, and supportive therapies may be needed to minimise them. Antiemetics should be prescribed according to the emetogenic potential of the chemotherapy.[14] Nausea and vomiting can continue for several days after a dose of chemotherapy and the duration of antiemetic therapy should take this into consideration. Guidelines exist for prescribing antiemetics with cancer chemotherapy.[15,16]

Blood counts need to be frequently checked with cytotoxic therapy. Patient monitoring, including laboratory tests and the parameters for initiating the next cycle of chemotherapy, should be clearly defined in the protocol or treatment plan. For example, a neutrophil count of greater than 1×10^9 is usually required for a cycle of cancer chemotherapy to proceed.

Particular care should be taken with patients when the cytotoxic therapy is taken continuously, for example cyclophosphamide or chlorambucil, as severe myelosuppression can develop. Cytotoxic chemotherapy can adversely affect liver and renal function and these should be monitored before each course of therapy.

Live vaccines are contraindicated in patients with impaired immune function which includes those receiving oral cytotoxic therapy. These vaccinations should usually be delayed until at least six months after the completion of any chemotherapy. Inactivated vaccines are generally safe, but patients may have a diminished immune response to the vaccine. The influenza vaccine should be administered before each influenza season and pneumococcal vaccine should be considered before starting therapy.

Recommendations

Despite the convenience that oral cytotoxic therapy offers, it carries the same risk of medication errors and adverse effects as parenteral therapy. Oral cytotoxic medicines have a narrow therapeutic index and monitoring the patient for safety and efficacy is essential. Written and verbal communication with patients and carers is critical for the safe and appropriate use of cytotoxic therapy.

If a patient unknown to the prescriber, pharmacist or healthcare professional presents for oral cytotoxic therapy, the risk of continuing therapy should be balanced against the risk of stopping therapy until a full history and safety checks are done. In many cases delaying therapy for a short time while a full patient review is conducted and laboratory counts are obtained is safer than continuing therapy. □

Dr Carrington served on advisory boards for Amgen and Merck Sharp & Dohme and has received honoraria from Roche and Merck Sharp & Dohme for educational presentations.

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Management of SLE in pregnancy

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease most frequently affecting women in their reproductive years. Fertility is not usually affected by the disease as autoimmune ovarian failure is rare, and most SLE patients become pregnant. Infertility in patients with SLE is usually due to drugs, especially cyclophosphamide. There is, however, emerging evidence of sub-fertility, possibly related to the presence of anti-phospholipid antibodies (aPL). Ovarian failure from cyclophosphamide is often related to total dose used and its use in patients over 35 years.

Outcomes of pregnancy in SLE

Twenty years ago women with SLE were advised against pregnancy. Today, circumstances have changed. In the USA, a national study recorded 13 555 deliveries in women with a diagnosis of SLE at discharge from 2000-2003, with a high maternal mortality. Risks of serious maternal complications such as pre-eclampsia, hypertension, bleeding and serious infections are listed in panel 1.

Panel 1. Maternal morbidity in SLE

- Pregnancy induced hypertension (PIH)
- Pre-eclampsia
- Gestational diabetes mellitus (GDM)
- Pulmonary hypertension
- Lupus flares
- Infections
- Renal failure
- Placental abruption
- Thrombophilia, deep vein thrombosis, pulmonary embolism
- Thrombocytopenia, hepatitis, HELLP syndrome
- Premature delivery and caesarian section

Planning a pregnancy with contraceptive use

Contraceptive use is lower in patients with SLE compared to women with no chronic illness in several studies, including one involving Sri Lankan patients. Unplanned pregnancies occurred significantly more in patients with SLE than in patients with rheumatoid arthritis or in women with no chronic illnesses. So planning for a pregnancy is essential in patients with SLE, for an optimal outcome. Although low dose hormonal contraceptive use has not been shown to lead to increased lupus flares for a period of up to one year in patients with inactive or mild disease activity, in moderate to severe disease activity and in prolonged use they may be associated with increased lupus flares. They may also be associated with increased thromboembolic risk, especially in the presence of aPL, and are best avoided. Although intrauterine contraceptive devices (IUCD) have led to increased risk of infections, especially in patients on immune suppressant medications, they are suitable for patients on minimal doses of immunosuppressives for long term use. Progesterone containing oral, injectable or implantable contraceptives are recommended in SLE for shorter periods, but use over 2 years may increase the risk of osteoporosis. Thus individualised contraceptive advice should be given to women with SLE. The benefits of preventing a pregnancy at an unsuitable time outweigh the risks associated with a chosen contraceptive in patients with SLE.

Pre-conception counseling

Having SLE is not a contra-indication for pregnancy. However, pregnancy should be avoided in the presence of pulmonary hypertension, renal failure or active SLE (panel 2). Disease should be in remission for at least 6 months before a pregnancy, so for a successful outcome, preconception counselling of patients is important. Tests to be done when planning pregnancy are given in panel 3.

Review of medication

Review of medications is a vital part of management during pre-pregnancy counselling. Drugs considered safe or having low risks compared to benefits are listed in Table 1. Published data show safety of hydroxy-

chloroquine in pregnancy and that discontinuation may lead to lupus flares. Cleft lip or palate in the baby with prednisolone was not shown in a prospective controlled study. Prednisolone may cause hypertension and infection and predispose to gestational diabetes (GDM) in mother, particularly when used in high doses. Azathioprine may be used to control disease activity, although it can cause in intra-uterine growth retardation (IUGR) and an increase pregnancy loss. Teratogenic drugs that need to be stopped, at least months before a pregnancy, and new drugs that should not be used (as safety data are not available) are also shown in Table 1.

Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided after 20 weeks of pregnancy because of risk of reversible oligohydramnios, premature closure of the patent ductus arteriosus, gastrointestinal bleeding, necrotising enterocolitis, pulmonary hypertension and prolongation of labour. Cylo-oxygenase 2 (COX 2) inhibitors should also be avoided for absence of data on safety and increased thrombotic risk. Antihypertensives should be reviewed, avoiding angiotensin converting enzyme inhibitors (ACEI), and angiotensin receptor blockers (ARBs) because of risk of renal dysfunction in the foetus. Switching to safer drugs such as nifedipine, methyldopa, and labetalol is essential.

Panel 2. Contra-indications for pregnancy in SLE

- Severe lupus flare within past 6 months
- Active lupus nephritis within past 6 months
- Stroke within past 6 months
- Previous severe pre-eclampsia or HELLP despite therapy
- Severe pulmonary hypertension (systolic pulmonary artery pressure >50 mmHg or symptomatic)
- Severe restrictive lung disease (forced vital capacity <1 litre)
- Chronic renal failure (creatinine level >2.8 mg/dl)
- Heart failure

(Abbreviations: HELLP, a syndrome characterised by haemolysis, elevated liver enzymes and low platelets; SLE, systemic lupus erythematosus, Adapted from reference 4)

Antenatal care

Antenatal care is ideally provided jointly by a multidisciplinary team. Patients should be referred early to an obstetric unit, where monthly follow up is indicated up to 28 weeks, every fortnight till 36 weeks,

Panel 3. Maternal and fetal monitoring in SLE

Tests to be done when planning pregnancy

- Renal function
- DsDNA level
- Lupus anticoagulant, aCL- IgG, IgM
- Complement – C3,C4
- Anti Ro/SS-A, Anti La/SS-B
- Liver function tests
- Full blood count – for platelets, haemoglobin, white cells

Tests for maternal risk during pregnancy

- DsDNA level by ELISA – once every trimester
- Serum creatinine or urea, and electrolytes
- Full blood count – for platelets, haemoglobin, white cells
- Liver function tests
- Serum uric acid
- Urine for proteins, and urine protein – creatinine ratio

Fetal monitoring

- Regular growth scans
- Doppler uterine artery blood flow at 20-24 weeks for predicting pre-eclampsia and IUGR
- Fetal scanning including fetal echocardiography if indicated
- Fetal movement monitoring and CTG if required

Table 1. Drugs for SLE during pregnancy

Drug class	Permitted	Contraindicated
Steroids	Prednisolone, pulse methylprednisolone Betamethasone, dexamethasone	NA
Antimalarials	Hydroxychloroquine	NA
Immunosuppressives	Azathioprine Cyclosporine Tacrolimus	Cyclophosphamide Mycophenolate mofetil Methotrexate Leflunomide Rituximab Belimumab
Antiplatelets	Aspirin	Ticlopidine Clopidogrel
Anticoagulants	Heparin	Warfarin
Antihypertensives	Methyldopa Labetalol Nifedipine Hydralazine (with caution) Beta-adrenergic blocking agents (with caution)	ACE inhibitors ARBs Diuretics
Analgesics and anti-inflammatory drugs	Acetaminophen NSAIDS (until week 32)	Cyclo-oxygenase inhibitors
Osteoporosis preventing treatments	Calcium supplements Vitamin D	Bisphosphonates

Abbreviations: ACE, angiotensin-converting-enzyme; ARB, angiotensin-receptor blocker; NA, not applicable; SLE, systemic lupus erythematosus. (Adapted from reference 4)

and weekly follow up thereafter. Tests for monitoring of disease activity are given in panel 3. Ds-DNA level by ELISA test, done once in every three months should guide to indications of disease activity. Complement components C3, C4 are unreliable as they usually rise during pregnancy, so that levels would be normal in a flare, or even low in the absence of a flare. Renal and hepatic function and full blood counts (FBC) including platelet counts are advisable. The fetal monitoring recommended is also given in panel 3. Careful monitoring for maternal complications are given in panel 1, and appropriate management are essential.

Lupus flares in pregnancy

SLE tends to flare in pregnancy and puerperium. Prospective studies with validated measures of disease activity have found a 2- to 3-fold increase in lupus disease activity during pregnancy. Most are mild with cutaneous and joint manifestations. Maternal flares have been associated with prematurity and active nephritis as an independent risk for fetal mortality. Signs and symptoms of normal pregnancy that must be differentiated from those of lupus flares are given in Table 2.

Management of lupus flares

Rash, arthritis and serositis are ideally treated with low dose steroids with or without hydroxy-chloroquine. Nervous system or renal flares need high dose prednisolone or intravenous methylprednisolone. During high dose steroid therapy, monitoring of blood pressure and blood

Table 2. Signs and symptoms of normal pregnancy that must be differentiated from those of SLE exacerbations

Pregnancy	SLE
1. Chloasma	1. Malar rash
2. Proteinuria secondary to pre-eclampsia	2. Proteinuria due to lupus nephritis
3. Pre-eclampsia	3. Renal disease due to an exacerbation of lupus
4. Thrombocytopenia in pregnancy (eg. HELLP syndrome)	4. Thrombocytopenia of lupus exacerbation (ie, TTP or ITP)
5. Pedal edema and fluid accumulation in joints (especially the knees) in the late stages of pregnancy	5. Arthritis of SLE

glucose are mandatory. Prednisolone is inactivated by the placenta, and less than 10% of the mother's blood prednisolone can reach fetus. While risk for the baby is less, reducing the dose as early as possible is necessary to minimise complications in the mother. Azathioprine can be used as a steroid-sparing agent. Prophylactic steroids do not lower the risk of flares or risk of side-effects such as premature rupture of membranes (PROM), infections, IUGR, hypertension, and GDM. The risks of these complications are greater than the benefits of prophylactic steroids. Cyclosporin is safe for the fetus, but there is risk of maternal nephrotoxicity. Tacrolimus, another calcineurin inhibitor that is 100 times more potent *in-vitro* compared to cyclosporin, is safe and effective for the treatment for lupus nephritis. Extensive experience in pregnant transplant patients has shown evidence of successful pregnancies without increased congenital abnormalities, compared with the general population. Intravenous immunoglobulin may be used for severe thrombocytopenia during pregnancy, and no fetal adverse effects have been reported.

Antiphospholipid (aPL) antibodies and SLE

About 30-40% of women with SLE have aPL antibodies. They may develop anti-phospholipid syndrome (APS) with recurrent pregnancy losses or present as subfertility. The diagnosis and management of obstetric anti-phospholipid syndrome was reviewed in a previous article and will not be described here. Patients with APS would benefit from treatment with aspirin and low molecular weight heparin (LMWH) for a successful pregnancy outcome.

Neonatal lupus

This is manifested in the presence of anti Ro/SS-A or anti La/SS-B antibodies. It is passively acquired from autoantibodies that cross the placenta. Usually this shows as a generalised rash in the neonate. Other features include haematological and hepatic abnormalities, or cardiac complications. The most dangerous manifestation of neonatal lupus is congenital heart block (CHB), which may occur in utero during the 2nd or 3rd trimester because of the binding of anti-Ro antibodies to the heart's conducting tissue and a resulting fibroid reaction. CHB occurs in 2% fetuses, a 24% mortality occurs by end of infancy, and most require a permanent pacemaker by 1 year. Recurrence of CHB has been noted 16% of subsequent pregnancies.

Complete CHB

This is irreversible and may be linked to in utero morbidity and mortality. Monitoring by serial fetal echocardiography is recommended starting at 18 weeks of pregnancy, if suspected. Early diagnosis of the CHB and its complications (pericardial/pleural effusion, myocarditis) usually avoids deterioration of fetal cardiac function. Dexamethasone and betamethasone, which are not inactivated by placenta, may be helpful as fetal treatment

Post-natal care

Risk of lupus flares is high during the post-natal period. Close monitoring is needed for at least one month after delivery, particularly for those who have had

recent activity. This is also a high risk period for thrombosis, especially if aPL is positive. In such patients, LMWH should be restarted and continued for 4-6 weeks.

Breast-feeding

Breast-feeding is recommended for most women with SLE. There is no increased risk of neonatal lupus related to breast-feeding. Most medications are now recommended to be continued during breast-feeding. Prednisolone under 20 mg/day, warfarin, and heparin appear to be safe. Hydroxychloroquine, azathioprine and cyclosporin also are now recommended during breast-feeding with recent data showing their safety. Avoiding breast-feeding for about 4 hours after taking medicines will significantly reduce the exposure of the baby to the drug.

Conclusions

Significant numbers of live births are now recorded in women with SLE. Pregnancies need to be planned for good outcomes. Appropriate use of contraceptives is essential. Pregnancy exacerbates SLE. Most patients with pregnancy losses have aPL, and aspirin and heparin in such patients improves foetal outcome. Some drugs earlier considered unsafe in pregnancy and breast-feeding are now regarded as safe. SLE is now a disease in which most patients can enjoy motherhood, with proper management.

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Self-assessment questions

Select the **best** response in each question

Question 1

A 21- year old sexually active university student presented to the NHSL outpatients' for increasing right-sided lower abdominal pain for 3 – 4 hours, preceded by two loose motions. She had nausea but no vomiting. She gave a history of two lower urinary tract infections (LUTIs) in the last 3 months, and had notes made 6 months ago by her G. P., querying irritable bowel syndrome.

Her oral temperature was 37.8°C, pulse 98 b.p.m., and she had tenderness in the right iliac fossa without rebound tenderness. Her WCC was 20.2×10^9/l, with neutrophils 15.2×10^9/l. Urine analysis showed no evidence of LUTI.

At this stage the most likely diagnosis is:

(A) mesenteric adenitis

(B) left ureteric colic

(C) acute appendicitis

(D) diarrhoeal episode of IBS

(E) ruptured ectopic pregnancy

Question 2

A 35-year old woman with multiple painful joint swellings and hypertension for one year, and a history of two pregnancy losses, is admitted to an obstetrics unit because she is pregnant (two missed periods), and the SHO detected an erythematous rash on her face with the characteristic butterfly distribution. She has been taking for 2 months the medications listed below on prescription. Which one of the following medications she is taking is safe to retain at this stage?

(A) Enalapril 5 mg bd

(B) Clopidogrel 75 mg/day

(C) Diclofenac potassium 25 mg tid

(D) Alendronic acid 10 mg/day

(E) Labetalol 100 mg bd

Answers to self-assessment questions

Question 1 (C). In the presence of fever, tenderness in the right iliac fossa, and a neutrophil leucocytosis acute appendicitis is the most likely diagnosis.

Question 2 (E). The only medication safe to retain is labetalol. The other four are unsafe in this ''precious pregnancy''. Appropriate adjustments are necessary for the hypertension, and for investigations indicated by the ''butterfly distribution'' facial rash.

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