Drug interactions and hormonal contraception

I saw a patient last week who attended for an implant removal because she wanted to conceive. She apologised for the scarring around her armpits, but the hidradenitis suppurativa had been much better since the dermatologist put her on rifampicin 9 months ago! Luckily, she hadn’t conceived…

With the increasing number of drugs on the market (e.g. HIV treatments) and the wider uses of existing drugs (e.g. anti-epileptics for migraine and neuropathic pain), we need to be aware of any interactions with contraception. This is particularly important because unintended pregnancy in some of these patients may be high risk.

Unfortunately, there is not a lot of good quality evidence on the effect of liver enzyme inducing drugs on hormonal contraception. However, the FSRH has reviewed what is available and published a number of guidance documents on drug interactions and contraception (FSRH CEU drug interactions with hormonal contraception 2012).

Pharmacokinetics

The cytochrome 450 enzyme system in the liver and small bowel metabolise ethinyloestradiol and progestogens into inactive metabolites which are excreted. So, any drugs which induce cytochrome 450 activity lead to increased metabolism of concurrent hormonal preparations. This potentially reduces hormonal bioavailability and contraceptive effect.

Enzyme inducing drugs act within 2d of initiation and their effect can last up to 4w after cessation, so extra or alternative contraceptive precautions must be continued for 4w after cessation.

Which drugs are enzyme inducers?

<table>
<thead>
<tr>
<th>Strong enzyme inducers</th>
<th>Moderate/weak enzyme inducers</th>
<th>NOT enzyme inducers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Topiramate</td>
<td>Benzodiazepines</td>
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<tr>
<td>Eslicarbazepine</td>
<td>St John’s wort</td>
<td>Gabapentin</td>
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<tr>
<td>Oxcarbazepine</td>
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<td>Pregabalin</td>
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<tr>
<td>Phenobarbital</td>
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<td>Lamotrigine (but see below)</td>
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<tr>
<td>Phenytoin</td>
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<td>Levetiracetam</td>
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<tr>
<td>Primidone</td>
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<td>Sodium valproate</td>
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<tr>
<td>Rifampicin</td>
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<tr>
<td>Rifabutin</td>
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<tr>
<td>Numerous HIV medications</td>
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</table>

Which contraceptive methods are probably affected by enzyme inducing drugs?

- Combined hormonal contraception (CHC).
- Progestosterone-only pill (POP).
- Subdermal implant (SDI): there have been reports of failures but no specific interaction studies have been performed.
- Ulipristal acetate (EllaOne, emergency contraception).
- Levonorgestrel 1500mg (Levonelle, emergency contraception).

Which contraceptive methods are not affected by enzyme inducing drugs?

- Progestosterone-only injectables (POI): the clearance of depot medroxyprogesterone acetate is roughly the rate of hepatic blood flow, so it is unlikely that its efficacy is reduced. This has been supported by studies on depot users taking anti-retrovirals.
- IUS: levonorgestrel has a localised effect which is unaffected by liver enzymes.
- IUD: non-hormonal methods are unaffected by liver enzymes.

How do I manage these patients in practice?

Switch them to a method which is unaffected by enzyme inducers such as a POI, IUD or IUS. If they are keen to continue their existing method, suggest the following:

Combined hormonal contraception

- Short term use of enzyme inducer (<2m):
  - Give a 30mcg monophasic 21d pill or Evra patch/Nuvaring.
  - Instruct the woman to use an extended regime (continuous pill taking until develops break-through bleeding for 3–4 consecutive days) or to tricycle packs.
  - She should also reduce hormone-free interval to 4d.
Also use additional contraception precautions (i.e. condoms) until 4w after enzyme inducer stopped. This regime should reduce chance of falling hormone levels leading to ovulation. Long-term use of enzyme inducers or does not wish to use condoms in addition to CHC:

- Prescribe total of 50mcg ethinyloestradiol or more (as a 20mcg + 30mcg pill, or 2 × 30mcg pills).
- The CEU recommends an extended or tricycling regime with reduced hormone-free interval.
- If break-through bleeding occurs, indicating possible low hormone concentrations, the dose can be titrated up in 10mcg increments to a total of 70mcg (2 × 35mcg pills per day).
- This is not recommended if a woman is taking very strong enzyme inducers, e.g. rifampicin.

I would not feel very comfortable prescribing doses of ethinyloestradiol >50mcg/day, especially as this practice is off-licence and there is no evidence for it!

**Progesterone-only pill or subdermal implant**

Offer additional POI for the duration of treatment and 28d after.

**Emergency contraception**

An IUD is the best option as both oral agents are potentially affected by enzyme inducers.

The CEU recommends that if an IUD is not suitable, give 3mg levonorgestrel (2 × 1500mcg tablets of Levonelle) as a stat dose within 120h of UPSI. There is limited evidence of efficacy. The same regime is recommended if HIV post-exposure prophylaxis for sexual exposure is given and emergency contraception is also required.

Ulipristal is not recommended because there is not enough data on it.

**Hormonal contraception and St John’s wort**

In March 2014, the MHRA issued a drug safety update in relation to the interaction between St John’s wort and hormonal contraceptives (DTB 2014;52:50).

- In 2013, the MHRA received two yellow card reports of women with the contraceptive implants Nexplanon and Implanon who had unplanned pregnancies after starting to take St John’s wort.
- There have been a total of 19 reported interactions with St John’s wort and hormonal contraception since 2000. This has resulted in 15 unplanned pregnancies and 4 cases of unscheduled bleeding.
- There is currently no data about any interaction with intrauterine devices.
- Information about the interaction with St John’s wort is included in the product information given with all hormonal contraceptives.

Isn’t there an issue with lamotrigine?

Lamotrigine is not an enzyme inducer so does not reduce the efficacy of hormonal contraception. However, studies have found that ethinyloestradiol increases lamotrigine clearance by inducing its metabolism, and therefore increases seizure potential in lamotrigine users on CHC. As a result, lamotrigine monotherapy has been designated a UKMEC 3 for CHC.

Sodium valproate inhibits the enzymes which metabolise lamotrigine and so counters the effect of ethinyloestradiol. As a result, if lamotrigine is given in conjunction with valproate as part of an anticonvulsant regime, CHC may be prescribed.

**Antibiotics and combined oral contraception**

The absence of any evidence of loss of contraceptive efficacy when broad-spectrum antibiotics are co-prescribed with the COCP led to the FSRH changing its guideline in 2011. Current FSRH guidance is that:

- No additional precautions are necessary when prescribing antibiotics to women using CHC.
- The exception is enzyme-inducing antibiotics such as rifampicin/rifabutin.
- Remind women that extra precautions are still required if they have diarrhoea or vomiting (treat as missed pills – see separate article in this chapter).
Drug interactions and hormonal contraception

- A drug history should be part of any contraception counselling, and remember to ask about St John’s wort!
- Remind patients to inform their doctors if they commence a new treatment because it may interfere with their contraception.
- All women starting enzyme inducing medication should be advised to use a contraceptive method which is unaffected by this medication.
- If a patient wishes to continue a method which is potentially affected by an enzyme inducer, advise condom use alongside their usual contraception.
- Higher doses of CHC may be prescribed off-licence to maintain efficacy.
- For emergency contraception, if an IUD is declined, 3mg of levonorgestrel may be given up to 120h off-licence.
- CHC should not be prescribed if a patient is on lamotrigine as an anticonvulsant monotherapy.
- Extra-precautions are no longer required when CHC users are prescribed antibiotics.

Do you ask about medicines as part of your contraception counselling?

How many of your female epileptics on enzyme inducing medication are on ‘safe’ contraception?

The following websites gives up-to-date information about current treatments and their interactions


HIV drug interaction charts: [www.hiv-druginteractions.org/Interactions.aspx](http://www.hiv-druginteractions.org/Interactions.aspx)

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature, and this should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular check drug doses, side effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages.

GP Update Limited
June 2017
All our courses are:

**Relevant**
Developed and presented by practising GPs and immediately relevant to clinical practice.

**Challenging**
Stimulating and thought-provoking.

**Unbiased**
Completely free from any pharmaceutical company sponsorship.

**Fun!**
Humorous and entertaining – without compromising the content!

Are they for me?

Our courses are designed for:

- GPs, trainers and appraisers preparing for appraisal and revalidation or wanting to keep up to date across the whole field of general practice.
- GP ST1, 2 & 3, looking for the perfect launch pad into general practice and help with AKT and CSA revision.
- GPs who want to be brought up to speed following maternity leave or a career break.
- General Practice Nurses, especially those seeing patients with chronic diseases.

What's included?

- 6 CPD credits in a lecture-based format, with plenty of time for interaction, humour and video clips, to keep you focussed and awake.
- A printed copy of the relevant handbook including the results of the most important research in primary care over the last 5 years and covering the subjects more extensively than possible in the course.
- 12 months' subscription to www.gpcpd.com. With three times the content of the handbook, it allows you to capture CPD credits as you read on the site and use it in consultations! It also comes with Focused Learning Activities - online learning activities to provide evidence for your appraisal and earn hundreds of further hours of CPD credits.
- Buffet lunch and refreshments throughout the day!

What's not included?

Our courses contain NO theorists, NO gurus, NO sponsors, NO reps on the day!
Just real-life GPs who will be back at the coal face as soon as the course has finished.

www.gp-update.co.uk
**The GP Update Course – our flagship course!**

With the amount of evidence and literature inundating us, it can be hard to know which bits should change our practice, and how.

The GP Update Course is designed to be very relevant to clinical practice and help you meet the requirements for revalidation.

We collate and synthesise the evidence for you so you don’t have to! Using a lecture based format, with plenty of time for interaction, the GP presenters discuss the results of the most important evidence and guidance, placing them in the context of what is already known about this topic. The presenters also concentrate on what it means to you and your patients in the consulting room tomorrow.

<table>
<thead>
<tr>
<th>Bristol</th>
<th>Wed 10 May</th>
<th>Cardiff</th>
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**Lead. Manage. Thrive! – The NEW management skills course for GPs**

Many of us have chosen to be salaried or portfolio GPs yet feel impotent or looked over when it comes to contributing to the effective running of our practices. We become frustrated and feel that we have little or no influence over what happens. It’s not your fault, most GPs (experienced and new) have had very little training in management and leadership skills for clinical practice.

Here’s the good news, all of us ‘lead’ whether in an official or unofficial role.

Who is this course for? GPs at every stage in their career who aren’t quite sure how to get unstuck! Also highly relevant to anyone who recognises the need to build their personal resilience and leadership skills to meet the demands of modern primary care, i.e. practice managers, nurses, and administrative and support teams.

As usual Red Whale has done all the legwork to bring you a concise, practical and actionable one-day course and handbook. Not only have we trawled through lots of relevant management, leadership and development literature, but we have also distilled its content through the lens of real GPs, enabling you to apply it to the reality of your practice.

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<tr>
<th>Newcastle</th>
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<td>Southampton</td>
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**The Women’s Health Update Course**

From the pill to pelvic pain, periods and prolapses, the one day Women’s Health Update course is a comprehensive guide to understanding and managing common gynaecological problems in general practice. Using a case-based approach will give you the skills to manage your female patients in a real surgery.

We aim to make the day fun, interactive as well as educational. You will leave the course feeling more confident, knowledgeable and with a much stronger pelvic floor!!!

The course is designed for all GPs and GP STs (male and female!) not just those with a special interest, however it does fulfill the CPD criteria for DFSRH/DFFP LoC IUD/SDI.

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<tr>
<th>Glasgow</th>
<th>Fri 9 June</th>
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<td>Manchester</td>
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The Cancer Update Course

Within the next 15 years the need for cancer care will double and you will look after as many cancer survivors as diabetics. Shared care follow up will become the norm, and secondary care will pass responsibility to us.

A key 2015 Lancet Oncology commission paper warned that: “GPs are inadequately trained and resourced to manage the growing demand for cancer care in high income countries”.

Education for GPs was one of their five key recommendations – we can help you get ahead of the curve! Established GPs and GP STs can use this course to bridge the gap in traditional GP cancer education which has focussed heavily on referral and end of life care missing out the whole journey in between.

This course is able to look in much more detail at the big picture behind the disease perhaps most feared by our patients and, let’s face it, that 1 in 2 of us will be diagnosed with over our lifetime.

Leeds  Thu 22 June
Newcastle  Fri 23 June
London  Thu 28 June
Birmingham  Fri 30 June
Nottingham  Thu 9 Nov

Manchester  Fri 10 Nov
Norwich  Wed 15 Nov
Exeter  Thur 16 Nov
London  Fri 17 Nov

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For more information on each course, please visit www.gp-update.co.uk/courses

The Effective Consultation Course

Manchester  Wed 10 May
London  Fri 12 May
Leeds  Wed 4 Oct

The Telephone Consultation Course

Leeds  Wed 17 May
Birmingham  Fri 19 May
London  Wed 7 June
Bristol  Fri 9 June

Manchester  Fri 13 Oct
London  Fri 6 Oct

Glasgow  Sat 4 Nov

The Medically Unexplained Symptoms Course

Manchester  Thur 18 May
London  Thur 19 Oct

Prices

GP Update Course:
GP £195 | GP Registrar £150 | Nurse £150
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- **Access to surveys and tools for your revalidation** – FourteenFish offers quick and simple to set up peer review and patient surveys to help you with revalidation.

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Sign up now - www.gp-update.co.uk/gpcpd

To book: online at www.gp-update.co.uk or call us on 0118 960 7077 or use the form below.

I would like to come on the following course(s) (please write legibly!):

- [ ] The GP Update Course (location) ............................................................... (date) ................................
- [ ] The Women’s Health Update Course (location) ............................................................... (date) ................................
- [ ] The Cancer Update Course (location) ............................................................... (date) ................................
- [ ] Lead. Manage. Thrive! Course (location) ............................................................... (date) ................................
- [ ] The Telephone Consultation Course (location) ............................................................... (date) ................................
- [ ] The Effective Consultation Course (location) ............................................................... (date) ................................
- [ ] The Medically Unexplained Symptoms Course (location) ............................................................... (date) ................................

I can’t attend a course, but would like to order your Handbook or DVD:

- [ ] GP Update Handbook and 12 months’ access to GPCPD £150
- [ ] GP Update Handbook, DVD and 12 months’ access to GPCPD £225
- [ ] Women’s Health Update Handbook £70
- [ ] Cancer Update Handbook £70

Name ................................................................................................................ Address ...........................................................................................................

Email ..................................................................................................................

(Please write your email address clearly as we’ll use it to send your confirmation letter and receipt.)

Price as stated in the flyer for each course. If applicable, please provide your discount code here.

Please send this form with your cheque payable to GP Update Limited to: Red Whale, University of Reading, Reading Enterprise Centre, Earley Gate Entrance, Whiteknights Road, Reading, Berkshire RG6 6BU

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