NEW MODELS OF HEALING

In a departure from PostScript's *usual focus on drug therapies, we have asked Dr David Reilly FRCP MRCGP FFHom, Consultant Physician at The Centre for Integrative Care in the Glasgow Homoeopathic Hospital, to provide his views on non-drug treatment and holistic approaches to chronic disease.*

We have to think differently in chronic disease. We are all realising that too often the drug 'fix it' model fails both the patients and the NHS, with the ever increasing drug bill which many feel leads to cuts in other areas of service. It is estimated that there are 3 to 4 million people on fluoxetine in the United Kingdom. This might be interpreted as reflecting a poverty of alternative models of care which could disillusion carers and patients alike. In a survey of all of Scotland's GPs, with a 62% return rate, 72% agreed that a failure to deliver holistic care in General Practice is leading, through expediency, to extra prescribing. 68% agreed that it is leading to extra secondary specialist referrals. The cost, side effects and missed opportunities this creates are critical. So what is another way of thinking of this issue?

One way has been complementary and alternative medicines (CAM), now used by 40% of people in any one year. CAM has made an important contribution and begun to change practice. For example, acupuncture is now widely used in pain clinics; a change unthinkable 20 years ago. But in chronic, complex problems, 'bolt on' CAM is *not* enough. This realisation led to the development of 'Integrated Care' (the meeting of orthodox and CAM approaches) and now, evolving from this, is 'Integrative Care' (of which more later).

The underlying flow of these changes in medicine is addressing not only the limits of the drug model but also the increased fragmentation and loss of holism. In parallel, scientific developments are underlining that conditions such as pain or depression should be considered as whole person experiences rather than as distinct entities that can be treated by prescribing. The emerging models do not emphasise the old fundamental aim of symptom elimination by external intervention, but focus instead on enhanced self-healing and self-coping capacity. We are changing our metaphors of healing from fixed to dynamic. If this sounds too nebulous, let me first describe some of the research findings which indicate the strength of that innate capacity, and make a few remarks on how it might be engaged.

Recent advances in brain scanning have shown dramatic discoveries related to self healing; phenomena previously often dismissed as placebo effect. Researchers reported in *Science* on patients in a double blind placebo controlled trial of an injected drug for Parkinson's Disease where brain scans monitored dopamine release. Many showed striking release of dopamine in response to placebo injections. This effect has now been replicated in single wired neurons in the brain. Others used quantitative EEG in an RCT of antidepressants. Those receiving active drug showed changes of activity in the left prefrontal cortex (the area of positive emotion) *but* so did patients responding to placebo! When these patients were told at the end of the study that they had been receiving placebo, the healing effect collapsed in all but a few cases and they had to go on to 'real' medicine.

PostScRxipt
from the
GGNHSB Area Drug & Therapeutics Committee
Issue 28 July 2005

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Website
http://www.show.scot.nhs.uk/ggnhsb/adtc

We are grossly underestimating the effects of context, expectation, ritual, trust and confidence in carers, and trust in the value of our interventions. These natural capacities, mobilised in a healing context, do not just enhance wellbeing, mood and, as a consequence, the pain experience; it has now been shown that such changes have marked impact on the immune system and organic disease process.

Chronic stress is seen as another significant issue. On the negative side, a recent meta-analysis of 300 studies has underlined the growing evidence that chronic stress can cause impaired immunity. On the positive side, can we learn to use these psycho-neuro-immune pathways to bring about creative change? In the last 25 years John Kabut Zin in America has developed the programme of 'Mindfulness Based Stress Reduction' (MBSR). In the UK, John Teasdale, a developer of Cognitive Behavioural Therapy (CBT), has combined it with MBSR as mindfulness-based CBT. This has been shown in randomised trials to reduce relapse in depression and has gained NICE approval.

The original programme was evolved in pain so there is wider potential for using this approach in different conditions. A recent study took individuals through an 8-week training course in mindfulness-based CBT and used a waiting list control group. All participants had brain scans before and after the eight week period and a flu vaccine at the end. Those receiving mindfulness-based CBT showed enhanced left prefrontal cortex activity and positive mood (similar to the antidepressant and placebo induced changes above). They also showed a correlated increase in the vigour of response to the flu vaccine.

This way of thinking calls for substantial changes in our approach and our services. The Centre for Integrative Care at the Glasgow Homoeopathic Hospital has been pioneering these areas for a number of years. It uses a model of innate capacity, a therapeutic engagement to begin to mobilise it, and support from non-toxic non-addictive interventions. Research data shows that substantial relief of suffering can be created which often breaks the costly spirals of further prescribing, investigations and specialist referrals. Some would see this as being 'only placebo' and others argue over

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Incremental alphabetical list of published SMC advice on which Glasgow decisions have recently been taken.
For further information and a full list of SMC advice, visit **www.scottishmedicines.org**

Drug	Reason for consideration	Indication/pharmacology	SMC decision	Glasgow decision
Adefovir dipivoxil (Hepsera®)	Resubmission	For the treatment of chronic hepatitis B in adults who have either: • compensated liver disease with evidence of active viral replication, persistently elevated serum alanine aminotransferase levels and histological evidence of active liver inflammation and fibrosis; or • decompensated liver disease.	Accepted for restricted use within NHS Scotland. Restricted to patients who demonstrate lamivudine resistance.	*Formulary.* Approved subject to review and production of protocol by Hepatitis C review group. SMC restrictions apply.
Anagrelide (Xagrid®)	New indication	Reduction of elevated platelet counts in at-risk patients with essential thrombocythaemia who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.	Not recommended for use within NHS Scotland.	Non-*Formulary.*
Candesartan cilexitil (Amias®)	New indication	Treatment of patients with heart failure and left ventricular systolic dysfunction (LVEF ≤ 40%) as add-on therapy to ACE inhibitors or when ACE inhibitors are not tolerated.	Accepted for use within NHS Scotland.	*Formulary.* Restricted to second line in patients who cannot tolerate an ACE inhibitor. Restricted to initiation by specialists for use as add-on therapy.
Eflornithine (Vaniqa®)	New medicine	Treatment of facial hirsutism in women.	Not recommended for use within NHS Scotland.	Non-*Formulary.*
Eplerenone (Inspra®)	Resubmission	Addition to standard therapy including beta-blockers, to reduce the risk of cardiovascular mortality and morbidity 3-14 days after myocardial infarction in stable patients with left ventricular dysfunction (LVEF ≤ 40%) and clinical evidence of heart failure.	Accepted for use in NHS Scotland.	Decision deferred for consultation with cardiology MCN.
Methylphenidate (Equasym XL®)	New formulation	For attention deficit hyperactivity disorder (ADHD) as part of a comprehensive treatment programme, when remedial measures alone prove insufficient.	Accepted for restricted use within NHS Scotland. Restricted as second line to be used only in exceptional circumstances where the supervising clinician has clear evidence that administration of a midday dose is problematic or inappropriate.	*Formulary.* Acknowledge new formulation. SMC restrictions apply.
Pegvisomant (Somavert®)	New medicine	Treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-1 concentrations or was not tolerated.	Not recommended for use within NHS Scotland	Non-*Formulary*
Triptorelin (Gonapeptyl Depot®)	New indication	Treatment of confirmed central precocious puberty in girls under nine years and boys under ten years.	Accepted for use within NHS Scotland	*Formulary.* Restricted to use under supervision of an appropriate specialist having facilities for the regular monitoring of response.
Valsartan (Diovan®)	New indication	To improve survival following myocardial infarction in clinically stable patients with signs, symptoms or radiological evidence of left ventricular failure or left ventricular systolic dysfunction.	Accepted for restricted use within NHS Scotland. Restricted to use as a second line alternative in patients who cannot tolerate an ACE inhibitor.	*Formulary.* SMC restrictions apply.
Ezetimibe (Ezetrol®)	ADTC appeal	Additional treatment choice for hyperlipidaemia patients not reaching target cholesterol levels with maximum tolerated statin dose.		*Formulary.* Restricted to initiation by specialists when cholesterol targets are not reached on the maximum tolerated statin therapy.
Fentanyl citrate (Actiq®)	ADTC appeal	Additional treatment choice for breakthrough pain in palliative care patients who might benefit from this mode of administration.		*Formulary.* Restricted to initiation by hospital palliative care and cancer specialists.

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Triptorelin (Decapeptyl®) SR 11.25mg for advanced prostate cancer

Triptorelin SR, a 3-monthly gonadorelin (GnRH) analogue preparation, has been added to the *Glasgow Formulary*. It previously received a positive SMC review.[1] It has been restricted to treatment of advanced prostate cancer in patients for whom the use of triptorelin is appropriate and who would benefit from reduced frequency of administration. The other GnRH analogues on the *Formulary* licensed for use in advanced prostate cancer are leuprorelin (Prostap®) and goserelin (Zoladex®). Both are available as monthly and three-monthly preparations.

Clinical trials have shown the monthly preparation of triptorelin to be at least as effective as leuprorelin in suppressing testosterone in patients with advanced prostate cancer. Results have also suggested monthly triptorelin to be similar to leuprorelin in terms of tolerability[2-4]. Additional unpublished data from the company show that the monthly and three-monthly preparations of triptorelin achieve equivalent testosterone suppression. No comparative trials of triptorelin with goserelin have been published.

The basic NHS costs for the three-monthly GnRH preparations have recently fallen. The table gives some comparative details for the available products.

	Triptorelin SR 11.25mg	Goserelin 10.8mg	Leuprorelin SR 11.25mg
NHS list price[5]	£207	£267.48	£376.20
Licensed dosing interval	Every 3 months	Every 84 days	Every 3 months
Annual cost	£828	£1,162	£1,505
Dosage form	Dry powder for reconstitution	Implant; ready for use	Dry powder for reconstitution
Route of administration	Intramuscular injection	Subcutaneous injection into anterior abdominal wall	Subcutaneous injection
Practical issues		Relatively large needle	

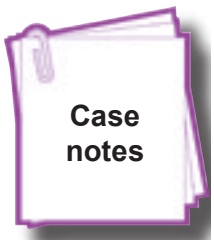
Buprenorphine (Transtec®) patches

The SMC has **not recommended** buprenorphine patches for treatment of moderate to severe cancer pain and severe pain which does not respond to non-opioid analgesics. No comparative data with alternative opioid preparations was provided so an adequate case was not made for its use as a cost minimisation option. Buprenorphine patches have not been added to the *Formulary*.

Buprenorphine acts as a partial agonist at μ opioid receptors and as an antagonist at κ opioid receptors. In the patch formulation the drug is held in a matrix system and absorbed through the skin at a constant rate. This is thought to provide stable serum levels. Minimum effective concentrations are reached in 12-24 hours, with maximum concentration at 59 hours. The patches are not suitable for acute pain.[1]

It is difficult to interpret the available studies of buprenorphine patches as they show only marginal benefit for active treatment over placebo.[2-4] A more convincing case could be made if the product was compared to alternative opioid preparations.

Adverse effects are those expected with opioid analgesics. Additional adverse effect such as erythema and pruritus are related to application of the patch. Buprenorphine interacts with any drug causing respiratory or CNS depression.



Fentanyl patches

Elayne Harris and Carolyn Mackay, Palliative Care Pharmacists, present a short case study illustrating some of the difficulties which can arise when prescribing fentanyl patches.

Mrs HV was being cared for at home following discharge from the local hospice. Oral anti-emetics and opioids had proved unsuitable and she was receiving a fentanyl patch (100micrograms/hour) and a syringe driver infusing haloperidol and cyclizine.

The district nurse (DN) visited at the weekend and found the patient to be in pain so administered 30mg oral oxycodone liquid. Her son was advised to contact the out of hours GP service if the pain persisted. He did so, and later that day she was visited by a doctor who doubled her fentanyl patch. He also left instructions for a syringe driver to be started with oxycodone 60mg/24hours and this was set up by the DNs that afternoon. When the DN visited the next day, the patient was extremely sleepy and had been agitated during the night.

In this case, Mrs HV had her patch dose doubled and had a syringe driver commenced with the equivalent of four breakthrough doses. In total, her daily opioid dose was increased by 166%. Mrs HV could have been commenced on a continuous subcutaneous infusion with the equivalent of 2-3 breakthrough doses of oxycodone (30-45mg/24hrs) without altering the dose of fentanyl patch. This would have increased her total daily dose of opioid by 30-50% and should have been adequate to treat her acute pain without precipitating toxicity.

Prescribing points

- Strong opioids should usually be increased in increments of 30-50%.
- Fentanyl patches should usually be increased in 25 microgram/hour increments. The case above had an increase of 100% (100 microgram/hour).
- Fentanyl patches are unsuitable for managing acute pain as any dose increases will take 24-48 hours to reach new steady-state plasma levels.
- For acute pain, administer oral immediate release opioids or, for those unable to tolerate the oral route, subcutaneous (SC) opioids, eg diamorphine.
- To calculate the breakthrough dose of SC diamorphine (mg):
  - Divide the fentanyl patch dose by 5, so for a dose of fentanyl 100 micrograms/hour, the breakthrough dose is 20mg SC diamorphine as required.
- To calculate the breakthrough dose of oral or SC oxycodone:
  - Calculate the diamorphine breakthrough dose as above (20mg)
  - Multiply by 3 to get equivalent oral dose of morphine (60mg)
  - Divide by 2 for breakthrough dose of oral oxycodone (30mg)
  - Divide by 2 for breakthrough dose of SC oxycodone (15mg).

Published studies and a 2004 audit in Glasgow hospitals and hospices show this is not an isolated case and that problems are not restricted to primary care. Issues identified locally included inappropriate starting dose of the patch and inadequate or no analgesia prescribed for breakthrough or at patch initiation. 10% of patients were given no breakthrough analgesia and almost 50% of patients were given inappropriate doses of breakthrough medication. In 71% of this latter group, doses were more than 25% outwith the recommended range which was deemed to be clinically relevant.

A number of algorithms for palliative care, including one for the effective and appropriate use of fentanyl patches, have been approved by ADTC. See **www.palliativecareglasgow.info/fentfacts** for more information.

News of *PostScript*

The next edition is nearer than you think! Following requests from the Prescribing Management Group and the ADTC, *PostScript* will now be produced every two months instead of quarterly. The blue and pink update sheets will no longer be circulated on paper, but will be available on local intranets.

New models of healing *contd from page 1*

the research base of individual complementary therapies. But the issue is far deeper; it is evolving a new model of care with a different purpose to the engagement and therapeutic encounter. This is 'Integrative Care' which aims to increase coherence within the individual and with their care.

Research suggests that forging a quality 'therapeutic alliance' is central in this, and an awareness of the stages of therapeutic process and of self-healing reaction become an inherent part of the care plan. We are familiar with the stages of grief from Kubler Ross, but the stages of recovery of well-being are less well studied. This emerging model from Glasgow has been used as the basis for developments in other countries. It is the first step of a new direction for research, education and care. Health carers want the human values of engagement, relationship and sparking of creative change to be seen as central to their work; not merely a backdrop to the 'real thing' of medication and procedures. We need a cultural change within medicine, and now we have the science to support it.

For those interested in further reading, a handout with background references and details of ways to learn more are available from **www.adhom.com**, *telephone 0141 337 1824 or davidreilly1@compuserve.com*

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Published by the Publications Sub-group to reflect the views of the Area Drug & Therapeutics Committee (ADTC) and NHS Greater Glasgow (GGNHSB). Invited opinion pieces reflect the views of the author and not necessarily those of the ADTC or GGNHSB.

Design, layout and production control:
Strathcashel Publications Project Management (01505 850 344)
Printed by: Core Image, East Kilbride