

# Details of the proposed new pharmacy contract for Scotland are revealed

BASIC details of the new contract for community pharmacy in Scotland were outlined last week.

In a joint letter sent to pharmacists on 31 July, the Scottish Executive Health Department and the Scottish Pharmaceutical General Council describe the progress to date. "The discussions are progressing well with agreement having been reached on the principles to underpin the new contract and on the service elements that the contract is expected to contain," it says.

Services will be divided into core and additional sections. Core services will be

provided by all community pharmacies. They are:

- A chronic medication service that will be based on repeat dispensing and pilot pharmaceutical care schemes in Scotland
- A minor ailments service, similar to the model piloted in Ayrshire and Tayside (see *P7*, 23 February 2002, p238)
- A public health service
- An acute medication service — dispensing medicines for acute illness



*A model pharmacy in Glasgow: the future of pharmacy?*

## Agreed principles

The Scottish Executive Health Department and the Scottish Pharmaceutical General Council have agreed a number of principles for the new community pharmacy contract. These include:

- Services will be provided that deliver pharmaceutical care efficiently and effectively
- A rational network of pharmacies/pharmacists that provides equitable and convenient access for patients will be supported
- Quality pharmaceutical care services will be properly resourced
- Opportunities for continuing professional development will be provided
- Premises will be fit for their purpose
- A suitable infrastructure will be put in place, including provision of information technology
- Financial turbulence for contractors will be minimised

Additional services will not necessarily be provided by every community pharmacy but instead by some contractors, perhaps acting together within a particular area. The additional services include extended hours provision, out-of-hours services, domiciliary oxygen, harm reduction services and advisory services to care homes. It is expected that a national framework and benchmark tariff will be agreed for these additional services.

There are two main differences between the proposed new contracts in Scotland and England, according to Frank Owens, chairman of the SPGC. First, a minor ailments service will be provided by all community pharmacies in Scotland. In England it seems more likely that this will be classified as an additional service (*P7*, 19 July, p77). The second difference is that although services will be divided into core and additional in Scotland, the aim is to avoid a two-tiered approach. He stresses that the services falling into the additional category are those

that do not need to be offered by every pharmacy and as such their provision can be agreed locally.

A framework setting out details of the services and the care standards expected is being developed. It is not until this work has been completed that discussions about remuneration will begin. However, the Scottish Executive has said that the new contract will not result in a detrimental effect on the global sum for pharmacy. Full implementation of the new contract is expected in 2005–06 but some phased introduction might begin next year.

Frank Owens offers pharmacists the following reassurance: "My personal view is that there will be no big bang associated with the introduction of the Scottish pharmacy contract," he told *The Journal*. "What we are seeking to do is to break down the contract into manageable, bite-size chunks and to phase in the necessary changes. That way we manage the change process better, minimising both financial and operational risk."

## Clarification sought on control of entry exemptions

THE Government has been asked to clarify what it means by two of the three exemptions it has proposed to pharmacy contract controls (*P7*, 26 July, p105).

Pharmaceutical Services Negotiating Committee chief executive Sue Sharpe has written to Rosie Winterton, the minister responsible for community pharmacy, to tell her that the PSNC considers the precise definition of a shopping centre over 15,000 sq m to be fundamental. Mrs Sharpe said that the PSNC had made no objection to the statement in the 2000 pharmacy plan that entry controls would be removed from large out-of-town shopping centres, such as Bluewater. But it now feared that a collection of shops in a suburban high street could satisfy the 15,000 sq m threshold and drive a coach and horses through the entry controls.

The other main area of concern relates to consortia formed to establish one-stop

primary care centres. The PSNC wants to know whether the consortium will be the primary care trust involved or the developers of the premises.

Mrs Sharpe's letter says that the PSNC relied on an assurance by Mrs Winterton's predecessor that PCTs should not provide community pharmacy services.

Mrs Sharpe goes on to say that it is bizarre to suggest that Balfour Beatty or any other developer could be given an incentive to expand into pharmacy services. She warns that only the larger pharmacy multiples would have sufficient resources to be involved in development consortiums and that the exemption seems to be discriminatory and risks creating new local monopolies.

The PSNC also wants to know exactly what a one-stop primary care centre is, given that a commonly used definition is a gen-

eral medical practice with a practice nurse plus at least one other health professional.

The letter suggests that the PSNC is anxious to move forward quickly on the new pharmacy contract, provided that the necessary definitions can be agreed first.

### ROYAL PHARMACEUTICAL SOCIETY NEWS

#### The Society and its members

An article by the President, Dr Gill Hawksworth, looks at what the Society delivers for its members (p187).

#### Book offers

The Pharmaceutical Press is offering summer discounts on 14 books (p190).

## Plans to widen PGDs to more health professions

PROPOSALS to allow dietitians, occupational therapists, prosthetists, orthotists and speech and language therapists sell, supply and administer medicines under patient group directions have been put forward in MLX294 by the Medicines and Healthcare products Regulatory Agency.

If accepted, these professions will be added to the list of professionals who are able to operate as named individuals under PGDs. The professions currently in that list are pharmacists, nurses, midwives, health visitors, optometrists, chiropodists/podiatrists, radiographers, orthoptists, physiotherapists and paramedics.

Anne Whateley, deputy chief executive of the Royal College of Speech and Language therapists, said that examples of medicines that speech therapists might need to use included topical anaesthetics following laryngoendoscopy or surgical voice restoration, antifungals and other medicines to relieve mouth ulcers or oral discomfort.

Prosthetists and orthotists might want to use botulinum toxin to treat unresponsive hyperhidrosis of the axillae, baclofen for cerebral palsy or flucloxacillin for soft tissue infections.

Arts therapists have been excluded from the proposal because their professional bodies have concluded that arts therapists have no need to be able to work with PGDs in their current professional practice.

PGDs can be used by the National Health Service, by charitable and voluntary health care organisations and in the armed force, prison and police health services.

Comments on the proposal can be sent to Anne Ryan, MHRA, 16-142 Market Towers, 1 Nine Elms Lane, London SW8 5NG (e-mail [anne-ryan@mhra.gsi.gov.uk](mailto:anne-ryan@mhra.gsi.gov.uk)) until 30 September. The consultation period is less than the usual 12 weeks because there has already been extensive informal consultation with the allied health professions' representatives.

## Protocol allows out-of-hours medicines for prisoners

PRISONERS in England will be able to request non-prescription analgesics or antacids when health care staff are not present under a new protocol developed by the Prison Health Service and the Department of Health.

At the request of a prisoner, prison officers will be able to issue packs containing either two tablets of a paracetamol/methionine combination product for treating pain or an antacid preparation for mild indigestion. A further request for a second dose can be made after four hours if health care staff are still not present. After this, on-call medical staff have to be informed. Prison officers are not allowed to recommend that a prisoner requests or takes any medicine. Prisoners must sign for each dose given.

Pharmacists and health care managers in prisons are responsible for implementing the protocol and for following up any requests made under it. Each prison will have to draw up its own version of the protocol, but they can only include the medicines listed above.

## Safer blister packs to start in October

ALL blister packed medicines that contain aspirin, paracetamol or iron will have to meet new British Standard BS8404 for non-recloseable child resistant packaging for medicines from October.

Following consultation by the Medicines and Healthcare products Regulatory Agency (*P7*, 30 November 2002, p767), the Medicines Commission has endorsed the proposal and had its advice accepted by the Government. Regulations which will come into force on 1 October are to be drafted. There will be a two-year transition period for medicines already on the market.

## Health food store cancer advice puts patients at risk

EMPLOYEES of health food stores could be putting patients with breast cancer at risk because the advice they give is not supported by sufficient evidence, a new study suggests. Furthermore, recommendations from store assistants are often unaccompanied by discussions about possible adverse effects of a product, or its potential interaction with conventional cancer treatments.

The authors of the study believe that action is needed: "Governing bodies should consider health food stores as commonly used, yet unregulated, sections of the health care system." They suggest that regulations are needed to protect vulnerable patients from the significant costs of purchasing products that lack evidence of benefit.

In the study, conducted by Dr Edward

Mills from the Canadian College of Naturopathic Medicine and colleagues from the University of Toronto and the University of Exeter, England, eight people trained to act as customers whose mothers were suffering from breast cancer, visited 34 Canadian stores. They browsed the store until approached by an employee and then asked for product recommendations, giving information about their mothers' treatment regimens only when asked.

The store employees recommended 33 different products, none of which was supported by evidence of effectiveness. Most employees (68 per cent) did not ask whether the patient was taking prescribed medicines. Only three (8.8 per cent) discussed the adverse effects of the products and only

eight employees (23.5 per cent) pointed out that the products might interact with prescribed drugs. Two employees suggested that the products might cure the breast cancer, and one recommended that one of the mothers should stop taking tamoxifen because it was "poisonous".

The study highlights the possibility that breast cancer patients are seeking advice and treatment from alternative sources. "Patients might not disclose this information to their traditional health care providers. However, the advice they seek could have a negative effect on their response to medical treatment and be the source of unexplained reactions," the researchers warn (*Breast Cancer Research* 2003;5:170).

# Derby scheme repeats success for pharmacy referrals for minor ailments

PHARMACY FIRST, a scheme in Derby for referring patients with minor ailments to see a pharmacist rather than a general practitioner, saved around 500 GP consultations a month. The scheme is the latest to demonstrate the benefits for patients and GPs of such services and comes as the merits of incorporating a national scheme in the new pharmacy contract are being debated.

Under the Central Derby Primary Care Trust scheme, patients from six inner-city GP practices could be referred by a receptionist to one of 11 pharmacies. The practices are in some of the most deprived areas of the city. As part of the referral, each patient was given a booklet listing the non-prescription medicines available under the scheme. If the patient visited a participating pharmacy, the pharmacist made a record in the book of any medicines prescribed. Medicines were given free of charge to patients exempt from National Health Service prescription charges. Pharmacies taking part in the scheme were paid an annual retainer of £50 and a consultation fee of £2.50 per patient visit. Medicines were reimbursed at Drug Tariff prices.

During a six-month audit in the second half of 2002, there were 3,686 referrals made. The average cost of medicines supplied for each referral was 75p. Adding pharmacy fees and PCT administration costs, the total cost was £11,982 or £3.51 per referral. No estimate was made of the costs

of the community pharmacists' time in carrying out the service.

Lisa Flint and Dr Peter Rivers of Research and Evaluation Services, University of Derby, analysed the scheme and say that pharmacists, GPs and patients all appreciated the service. They recommend that it should be extended to other practices and pharmacies. Some of the areas for development identified include extending the formulary of medicines and reducing the amount of paperwork associated with the scheme. Concerns were expressed by pharmacists and their staff that they felt under pressure to prescribe medicines to all patients referred to them and that some patients had used the scheme to get medicines even though they were not entitled to do so.

At the same time, the Pharmaceutical Services Negotiating Committee is continuing to press for a similar scheme to be included as part of the new national pharmacy contract. The PSNC wants this to be one of the core, or essential, parts of the contract. The Department of Health currently favours making such a scheme an additional service that PCTs can choose to implement locally if desired. The Department is understood to be concerned about the cost implications of any nationally promoted scheme.

Alistair Buxton, head of NHS services at the PSNC, told *The Journal*: "All the

schemes similar to the one in Derby that we are aware of have not increased the cost of prescribing medicines."

In Scotland, it has been agreed in principle to make a minor ailments scheme a core part of the new community pharmacy contract (see p165).

## Medicines implicated in over 6 per cent of acute hospital admissions

PATIENT admissions to an acute medical unit in Nottingham over a six-month period were related to medicines in over 6 per cent of cases and of these, two-thirds were preventable, a study has shown (*Quality and Safety in Health Care* 2003;12:280).

The authors of the research believe the preventable drug-related admissions were predictable, raising concerns about the level of medicines management in primary care.

Based on their findings, they suggest that it may be worth focusing on preventing morbidity associated with non-steroidal anti-inflammatory drugs and low-dose aspirin. They recommend that patients at high risk of gastrointestinal bleeds are monitored and that general practitioners prescribe ulcer-healing drugs at the same time to prevent adverse effects.

The study involved 4,093 patients admitted to the medical admissions unit at Queen's Medical Centre, Nottingham, who were seen by a pharmacist. Drug-related morbidity was judged to be the cause of 265 (6.5 per cent) of these admissions and 178 (67 per cent) of these were thought to be preventable.

In addition to NSAIDs and anti-platelets, beta-blockers, antiepileptics, diuretics, sulphonylureas, digoxin, inhaled corticosteroids, nitrates and insulin were implicated in the drug-related admissions. Most were attributed to problems with prescribing (35 per cent), monitoring (26 per cent) and patient adherence to their regimens (30 per cent).

Veronica Wray of PharmacyHealthLink told *The Journal* the research highlighted the need for GPs to work more closely with pharmacists.

"I think that all the pharmacy organisations would agree on this issue. There's a real need for local practitioners to work together for the benefit of patients and to forget all the professions' territorial behaviour. The push for this must come at an undergraduate level," she said.

The finding that 67 per cent of drug-related hospital admissions could have been prevented is tragic, she added. "A huge percentage like this, multiplied nation wide, means millions of pounds wasted every week plus wards full of people who shouldn't be there."

## Reading joins rush to open a new school of pharmacy

THE University of Reading has become the sixth English university in the past two years to state an intention to open a new school of pharmacy. It hopes to take its first students in October 2005.

The university says that it is geographically well placed to offer a master of pharmacy degree because this course is not currently taught at any institutions in Berkshire, Buckinghamshire or Oxfordshire. The nearest schools of pharmacy are in London, Portsmouth and Bath.

The Reading school will provide undergraduate education and postgraduate research. The university also intends for it to serve as a regional centre for postgraduate education for pharmacists and technicians in the Thames Valley area. The university currently has research and teaching departments in biomedical sciences, medicinal chemistry, nutraceuticals, food biosciences and plant sciences.

The project is being led by Professor Gavin Brooks, MRPharmS, professor of cardiovascular research at the university, who is likely to head the new school.

# AstraZeneca accused of patent abuse

ASTRAZENECA has been accused by the European Commission of misusing European government procedures to delay the introduction of generic competition to Losec (omeprazole).

The commission says that AstraZeneca sought extensions to its patents for Losec that it was not entitled to. Supplementary protection certificates (SPCs) can be granted by patent offices to extend patent lives by up to five years to take into account the prolonged development time for pharmaceuticals between filing a patent and gaining marketing authorisation. Such SPCs are only available for products marketed in Europe after certain cut-off dates. The EC says that AstraZeneca deliberately

misrepresented the first date of authorisation for Losec to gain extra protection.

Additionally, the EC says that requests to deregister marketing authorisations for the original capsule form of Losec when a tablet formulation was launched were intended to stop generic manufacturers and parallel importers obtaining licences since, in principle, these are only granted in relation to an existing authorisations.

The EC's statement of objections marks the opening of a formal investigation. The company will be able to make its defence in writing or at oral hearings.

In a statement issued on 31 July, AstraZeneca said it would vigorously refute any alleged wrongdoing.



EC says AstraZeneca got patent extensions on false pretences

## Hospital pharmacy vacancy rate falls slightly but remains high

SIX per cent of hospital pharmacy posts in England had been vacant for at least three months in March 2003, according to figures from the Department of Health. The vacancy rate had fallen from 6.6 per cent in 2002 but the number of vacancies had increased by six to 286 whole-time equivalents (WTEs).

The annual survey of National Health Service vacancies reveals wide variations in unfilled posts across England. The highest vacancy rate was 16.6 per cent in the Bedfordshire and Hertfordshire Strategic Health Authority area (21 WTEs). The lowest was 0.8 per cent (2 WTEs) in West Yorkshire. For pharmacy technicians, the overall picture was similar. The vacancy rate fell slightly to 2.6 per cent but the number of vacant posts rose from 120 WTEs to 131. The highest vacancy rate was 10.4 per cent in North Central London.

In 2003, nine preregistration trainee posts were unfilled compared with 10 the previous year.

Helen Remington, chief pharmacist at Addenbrooke's NHS Trust, commented:

"The published new vacancy figures indicate that little progress has been made on vacancies. Everything must be done to ensure that this position improves over the next few years. New schools of pharmacy will provide additional pharmacists, but not yet.

"The immediate target is to ensure salaries attract staff to the service. The NHS is already paying high costs for locum staff to fill the vacancies and the logic is inescapable — recruit permanent staff at an economic rate and reduce the expensive use of temporary staff."

Mrs Remington said that the vacancy rate put pressure on existing work and jeopardised the expansion of pharmacists' work into new areas, such as improving antibiotic prescribing and pharmacist prescribing, which would improve patient services.

□ **Welsh vacancies** The three-month vacancy rate for hospital pharmacist posts in Wales fell by more than half in 2003. At the end of March, there was a 2.4 per cent vacancy rate (8 WTEs) compared with 4.9 per cent (17.3 WTEs) the year before.

## NICE reviews its appraisal process

PHARMACISTS and other health care professionals are being invited to comment on how the National Institute for Clinical Excellence conducts its appraisals. NICE is reviewing the methods used in its technology appraisal programme and has published two consultation documents.

The first document entitled "Guide to the technology appraisal process" describes how health care professionals and other stakeholders can contribute to appraisals. The main changes include earlier involvement in setting the scope of the appraisal, making more documents used in appraisals available to the public and providing more clarity about when and how NICE will update its guidance.

The second document — "Guide to the methods of technology appraisal" — describes the methods used by NICE for health technology assessments. The updated document offers a more detailed statement of what evidence of clinical and cost effectiveness is needed and how it is interpreted by NICE appraisal committees.

Links to the documents can be found on *PJ Online* ([www.pjonline.com/links/pj](http://www.pjonline.com/links/pj)).

## Supplementary prescribing training

PHARMACISTS wishing to find out more about the supplementary prescribing course at London Metropolitan University can attend a presentation at the university on 13 August at 3pm. Places can be booked via the admissions hotline (tel 020 7133 5005).

The LMU is one of five universities to be accredited so far to provide a supplementary prescribing course. The others are Keele University, Robert Gordon University in Aberdeen, Homerton College in Cambridge and King's College London. Further information about the courses will be published in the next issue of *Prescribing and Medicines Management*.

### PJ Online

*PJ Online* contains the editorial contents of *PJ* publications.

#### Citation searches

The contents pages (for 1999 and 2003) of the online *Pharmaceutical Journal* now contain page numbers. Thus, items can be found where the citations are known. The contents pages for 2000 to 2002 are being gradually updated, and other journals will be added in due course.  
[www.pjonline.com/backissues](http://www.pjonline.com/backissues)

#### Medicines requiring storage at low temperature in the pharmacy

A list prepared by the Royal Pharmaceuti-

cal Society's technical information centre, together with storage advice and contact details for further help.  
[www.pjonline.com/pip](http://www.pjonline.com/pip)

#### Support and services

Information on services provided by the Royal Pharmaceutical Society, including

- Benevolent fund
  - Birdsgrove House
  - Health support scheme
  - Legal information
  - Library
  - Technical information service
- [www.pjonline.com/services](http://www.pjonline.com/services)  
[www.pjonline.com/support](http://www.pjonline.com/support)

## BRIEFLY

**Dioralyte Relief to be GSL**

Aventis has applied for its raspberry and blackcurrant flavoured Dioralyte Relief products to be reclassified as general sale list medicines. Dioralyte has been a GSL medicine for some time. Dioralyte Relief differs from Dioralyte in that it contains mainly precooked rice powder instead of glucose. Consultation on the application closes on 5 September.

**Heroin prescribed for addicts**

Two randomised controlled trials have found that co-prescription of inhaled heroin with methadone is more effective than methadone treatment alone, and probably just as safe. Researchers report considerable improvements in physical and mental condition and social functioning of addicts prescribed a combination of heroin and methadone, including substantial reductions in criminal behaviour, with few serious adverse effects (*BMJ* 2003;327:310).

**Paclitaxel useful in lung cancer**

A triple therapy regimen of paclitaxel (Taxol), etoposide and carboplatin appears to improve survival in patients with small-cell lung cancer when compared with a regimen of etoposide, carboplatin and vincristine. Tumour response rates for the two regimens were similar. However, the three-year survival rate for patients in the paclitaxel group was 17 per cent compared with 9 per cent for patients in the vincristine group (*Journal of the National Cancer Institute* 2003;95:1118).

**Betel and areca are carcinogenic**

Chewing betel quid, even without tobacco, is carcinogenic to humans, says the International Agency for Research on Cancer following an evaluation of published studies. The agency also concludes that the areca nut, a component of betel quid and other products that are chewed, is carcinogenic. Betel quid generally consists of betel leaf (from the Piper betel vine), areca nut (from the Areca catechu tree), and slaked lime (predominantly calcium hydroxide), to which tobacco is often added.

**Web-based smoking cessation plan**

An online smoking cessation programme tailored to individuals has helped more people give up smoking than a non-tailored programme, says GlaxoSmith-Kline. In a trial, 3,971 smokers were randomised to either the Committed Quitters stop smoking plan (CQ Plan) or a non-tailored plan. Of those assigned to the CQ plan, 55.4 per cent were able to sustain 10 weeks' continuous abstinence from smoking, compared with 43.3 per cent of those using the non-tailored plan. Data were presented at the World Conference on Tobacco or Health in Helsinki this week.

# Genetic test predicts how breast cancer responds

GENE expression profiles could be used to determine whether patients with breast cancer will respond to docetaxel (Taxotere), researchers report (*Lancet* 2003;362:362). Patients likely to be resistant to the drug could be identified using this technique and this would reduce the need for unnecessary treatment, they say.

Dr Jenny Chang and colleagues from Baylor College of Medicine, Texas, took biopsy samples from primary breast tumours in 24 patients before treatment and then assessed tumour response to docetaxel.

They found that different gene expression profiles were associated with different responses to the drug — in all, 92 genes correlated with docetaxel response. Genes involved in the cell cycle, protein transport and protein modification were expressed more in tumours sensitive to treatment. Resistant tumours showed increased expression of some transcriptional and signal transduction genes.

Dr Chang comments: "This study helps to define the molecular portrait of cancers

that respond or not to docetaxel, one of the most active agents in breast cancer treatment. When validated, this type of molecular profiling could have important implications in defining the optimum treatment for individual patients, and reduce unproductive treatment, unnecessary toxicity, and overall cost."

## Use of HRT linked to 20,000 extra breast cancers over past decade

THE use of hormone replacement therapy (HRT) has resulted in an estimated 20,000 extra breast cancers in the United Kingdom over the past decade, say researchers. Of these, 15,000 were associated with use of products containing a combination of oestrogen and progesterone (*Lancet* 2003; 362:419).

The researchers point out that the main reason for using combination products is because of the increased risk of endometrial cancer associated with unopposed oestrogen. "However . . . there seems to be little

advantage to using oestrogen-progesterone in preference to oestrogen-only HRT for women who still have a uterus," they say.

The authors of an accompanying editorial recommend that women taking HRT should discontinue therapy and that guidelines for care of postmenopausal women need to be rewritten.

□ **Coronary heart disease risk** Final results on HRT use and coronary heart disease risk from the Woman's Health Initiative are published this week (*New England Journal of Medicine* (2003;349:523)).

## MeReC says role for new topical eczema treatments is limited

ATOPIC eczema can be controlled in most patients through the avoidance of exacerbating factors, and the use of emollients, topical corticosteroids and, where indicated, oral antibiotics, according to the latest issue of *MeReC Bulletin*. The topical immunosuppressive agent tacrolimus (Protopic) should be reserved for second-line treatment in certain circumstances (eg, when stronger corticosteroids are needed most of the time or for use on the face). Evidence for pimecrolimus (Elidel) is insufficient, it adds.

The bulletin can be downloaded from the National Prescribing Centre website ([www.npc.co.uk](http://www.npc.co.uk)).

## Triple therapy linked to non-response in patients with HIV

NEW triple therapy regimens for patients infected with HIV should not consist of the combination abacavir (Ziagen), lamivudine (Epivir) and tenofovir (Viread), the European Agency for the Evaluation of Medicinal Products has warned. Any patients already receiving this combination should be monitored frequently for signs of viral load increase. The advice is particularly important for once-daily regimens, says the EMEA.

The warning follows reports of a high rate of early non-response in treatment-naïve patients given this combination of drugs as part of a clinical trial. The reasons for the observed non-response are not known.

# Antibody useful in renal-cell cancer

A NEW treatment option for patients with metastatic renal cancer has shown promise in a phase II trial.

Bevacizumab is a neutralising antibody against vascular endothelial growth factor and appears to prolong time to disease progression in patients with metastatic renal-cell cancer. Researchers from the United States National Cancer Institute, Bethesda, Maryland, compared the drug with placebo in 116 patients. Bevacizumab was given at one of two doses — 3 and 10mg per kg of body weight, given every two weeks as an intravenous infusion.

Time to disease progression was, on average, 2.3 months longer for patients given high-dose antibody than for patients given placebo. In addition, more patients assigned to the high-dose group than to placebo were disease free four months and

eight months after the start of the trial (64 per cent compared with 20 per cent and 30 per cent compared with 5 per cent, respectively).

The researchers say that although bevacizumab had only a small clinical benefit, the effects were likely to be due to true biological activity. Earlier *in vitro* data suggest that the drug's antitumour effects are due to inhibition of angiogenesis.

They suggest that future treatments for renal cancer that target angiogenic mechanisms should consider pathways other than the one mediated by vascular endothelial growth factor. "It is likely that the future of angiogenic therapy will require a rational combination of inhibitors, directed by a better understanding of the biology of each individual type of cancer," they conclude (*New England Journal of Medicine* 2003;349:427).

## Inhaled apomorphine promising for erectile dysfunction treatment

AN INHALED form of apomorphine has shown promise as a fast-acting treatment for erectile dysfunction.

Developed by Vectura, VR004 is a breath actuated, dry-powder inhaler device containing apomorphine hydrochloride. New clinical trial data have shown that it could produce an erection sufficient for intercourse as soon as three minutes after dosing.

In Phase IIa clinical trials doses of 200µg, 400µg and 800µg were administered to 35 patients with mild to moderate erectile dysfunction in a placebo controlled, escalating dose design. Erectile performance was assessed in response to visual stimuli in a clinic setting using a modified version of the international index of erectile function questionnaire. Erections of sufficient quality for intercourse were achieved by 59 per cent of patients receiving 800µg apomorphine and 49 per cent of patients receiving 400µg com-

pared to 31 per cent of patients receiving placebo. The response rate for patients receiving 200µg was 23 per cent. The median time for onset of erection was eight minutes following administration of 400µg and 800µg doses, the most rapid response rate being three minutes. Vectura states that the drug was well tolerated, with no serious or severe adverse events reported.

The company expects that the inhalation route will prove more efficient than oral, sublingual or intranasal delivery by avoiding first-pass metabolism, requiring lower doses of active drug and providing a faster onset of therapeutic activity.

□ **Topical treatments** Futura Medical has completed a phase II study of a rub-on vasodilator cream for the treatment of male erectile dysfunction. They are also developing a condom that incorporates an erection-enhancing compound.

## Histone deacetylase inhibitor may prevent pre-term labour in women

PRE-TERM labour in women could be prevented using a histone deacetylase inhibitor to alter progesterone receptors, say researchers from the University of Texas Southwestern Medical Centre, Dallas.

The researchers have found a way to delay pregnant mice from going into labour for 24–48 hours. This is significant since the average length of gestation in the mouse is only 19 days, and the authors say that the biochemical steps associated with labour are likely to be the same in mice and humans.

Elevated progesterone levels prevent the uterus from contracting throughout a normal pregnancy. The researchers postulate that labour is caused by a number of fac-

tors that prevent progesterone from acting. They examined tissues taken from the myometria of women at the end of pregnancy and in labour, and found a marked decline in proteins containing histone acetylase activity at this time. Such activity alters the structure around progesterone-responsive genes, antagonising progesterone receptor function. The researchers found that administration of trichostatin A, a specific and potent histone deacetylase inhibitor, to pregnant mice in late gestation increased histone acetylation in the uterus, allowing the progesterone receptors to continue functioning (*Proceedings of the National Academy of Sciences* 2003;100:9518).

## Protein helps HIV avoid antiretrovirals

A PROTEIN expressed by HIV-1 has been shown to stimulate host cells in such a way that the virus is able to set up viral reservoirs and "hide" from antiretroviral therapy.

At one time it was thought that HIV-1 could attack only replicating CD4+T-cells, but it is now known that the virus can infect T-cells even when they are in their inactive state. HIV-1 in these cells is not destroyed by current antiretrovirals, but forms persistent reservoirs in the body, re-emerging when antiviral therapy stops.

Researchers from the University of Massachusetts medical school showed that the viral protein HIV-1 Nef interacts with infected macrophages leading to increased production of two soluble factors, sCD23 and sICAM-1. In turn, these factors stimulate the production of surface molecules on B-cells, which, upon contact with inactive T-cells, render the T-cells vulnerable to HIV-1 infection. The researchers propose that it is the activity of Nef that permits infection of resting cells by HIV-1. Interruption of this process could inhibit the formation of cellular reservoirs of HIV-1 cells (*Nature* 2003;424:213).

### BRIEFLY

#### Pleural mesothelioma hope

Patients with pleural mesothelioma survive longer and experience less pain and shortness of breath when treated with cisplatin and pemetrexed. In a study of 456 patients, this combination caused tumours to shrink in 41 per cent of patients compared with 17 per cent of patients given cisplatin alone. Addition of folic acid and vitamin B<sub>12</sub> reduced toxicity associated with pemetrexed (*Journal of Clinical Oncology* 2003;21:2636).