

Welsh Assembly earmarks £500,000 for automated dispensing in hospitals

THE National Assembly for Wales is to spend £500,000 installing automated dispensing robots at three hospital pharmacies in the next financial year. The move is the first phase in a plan that could see robots installed in all hospital pharmacies in Wales.

Jeremy Savage, chief pharmacist at West Wales General Hospital, Carmarthen, is one of the architects of the move to automated dispensing. He told *The Journal* that following a meeting with Welsh Health Minister Jane Hutt, the Welsh Chief Pharmacists Committee put forward proposals including automated dispensing. Following intensive lobbying of the Assembly, in conjunction with the Royal Pharmaceutical Society's Welsh Executive, Mr Savage was asked to write a three-phase implementation plan for automated dispensing.

Cheryl Way, principal pharmacist at Llandough Hospital, one of the pilot sites, said that one of the main requirements for automated dispensing to work is a move to patient packs and a greater use of patients' own drugs. Llandough Hospital hopes to use its robot for both inpatient and outpatient dispensing and ward box assembly.

"This will release staff time and we hope it will allow our pharmacy technicians to spend more time working on the wards. We want to undertake more assessments of



Installing automated dispensing systems can allow pharmacy staff to spend more time on wards

patients' medication on admission and spend more time with patients at discharge, making sure they have the correct medicines and that they understand how to use them. We are doing this already, but we could do more if we had more time — automated dispensing will help a lot."

Speaking during a visit to Llandough Hospital, which is in her constituency, Jane

Hutt said: "There are substantial benefits to the new automated dispensing systems. A report by the United States National Academy of Science estimated that over 78 per cent of dispensing errors could be avoided by the use of automated dispensing systems. In addition though, the automated system will enhance the benefit of pharmaceutical care by releasing staff from the dispensary to the patient's bedside. This will reduce the incidence of prescribing and administration errors thereby improving patient outcomes and reducing costs."

A study published in *The Journal* last year (30 March 2002, p437) showed that installing automated dispensing at Wirral Hospital, Merseyside, allowed 3.5 whole-time-equivalents of pharmacy staff to be redeployed from dispensary to ward work while turnaround times in the dispensary were maintained or improved. One of the article's authors, Ann Slee, is now chief pharmacist at Glan Clwyd Hospital, which has been chosen as the third pilot site for automated dispensing.

Comment, p38

Three-phase rollout planned for automation

The three hospitals selected for the first wave are Llandough Hospital, Cardiff, West Wales General Hospital, Carmarthen, and Glan Clwyd Hospital, Bodelwyddan.

The three hospitals were chosen as pilot sites because they are most suitable for early installation of robotic equipment. Each is a district general hospital with around 450–550 beds. An official notice inviting tenders for the scheme is to be published shortly. It is expected that the first robot could be installed in April or May with the other two following in June or July.

A second phase would see automated dispensing at a further eight hospitals in the following financial year, subject to approval by the Assembly. The remaining 11 hospitals in Wales would follow after that, subject to any changes needed to take account of specialist services, such as mental health, where patient pack dispensing is not the norm.

Ricin found by police during raids on flats in London

RICIN, a protein toxin derived from the beans of the castor oil plant, was discovered by officers from the Metropolitan Police anti-terrorism branch during raids on premises in north and east London on 5 January. One of the flats raided was above Guardian Pharmacy in Wood Green. The pharmacy has no connection with the flats.

The Metropolitan Police and the Department of Health said in a joint statement issued on 8 January that a small amount of the material found at Wood Green had tested positive for the presence of ricin. Police said that investigations are continuing and called on the public to

remain vigilant and to report anything suspicious.

Department of Health guidance being sent to National Health Service organisations and pharmacy groups says that ricin inhibits protein synthesis and has widespread toxic effects on the body. These include damage to most organ systems and a combination of pulmonary, liver, renal and immunological failure may lead to death.

Early symptoms of ricin poisoning depend on the route of administration. They include fever, gastrointestinal upset and coughing. Absorption via the lungs as a result of exposure to aerosolised toxin leads

to particularly serious lung damage including pulmonary oedema and adult respiratory distress syndrome. Ingestion of ricin causes irritation of the gut. The fatal dose by injection is thought to be around 1µg/kg.

Information on treating patients who may have deliberately been exposed to ricin can be found on the Public Health Laboratory Service website. A link can be found on the *Pf Online* links page (www.pfonline.com/links). There is no antidote to ricin and only symptomatic and supportive treatment can be given. The effects of exposure to ricin may be delayed for some hours after exposure occurs.

Department of Health's skill mix paper shows limited vision, the PSNC says

THE Pharmaceutical Services Negotiating Committee has dismissed the Department of Health's skill mix discussion paper as showing little vision of how pharmacists' skills can be used to deliver better care through the National Health Service.

Although the skill mix paper asserts a commitment to a strong and developing community pharmacy service, the PSNC response says that there is nothing in it, or elsewhere in Government policy, that sets out how this commitment will be implemented.

The PSNC wants to see a new national contract supplemented by locally negotiated services to meet specific health needs and local priorities. It takes the view that development of the pharmaceutical service will be frustrated if new services are not set in the framework of a national contract. Par-

ticular developments that the PSNC wants to see are the introduction of free non-prescription medicines for people who cannot afford to buy them and community pharmacy-based medication reviews.

"We can see no sense in developing medication review within primary care centres, rather than community pharmacy," the PSNC says.

One reason for this, which the PSNC also cites in opposition to keeping pharmacies open when pharmacists are absent, is the congregation of primary care practitioners in large health centres, which forces patients to travel further, and for longer, to get health care.

"As Government commitment to a strong and developing community pharmacy service becomes manifest we should ensure that the services are available from

every community pharmacy," the PSNC says. "Today, the community pharmacist is the only instantly accessible health care practitioner."

Proposals to delegate dispensing to appropriately trained and regulated staff meet with PSNC approval. It says that regulation should include conduct and discipline, as well as training and continuing professional development. To achieve delegation, the PSNC supports reinterpretation of the requirement in the Medicines Act 1968 for pharmacists to supervise dispensing, not its abolition. That pharmacists should have to be present at some point between the receipt of a prescription and the handing over of dispensed medicines is the PSNC view. It points out that there is no definition of the meaning of supervision in the Medicines Act or in any case law.

Staff shortages hold back skill mix developments, says UNISON

SHORTAGES of hospital pharmacy staff are holding back the developments outlined in the Department of Health's skill mix consultation paper, according to UNISON, which represents the majority of National Health Service pharmacy technicians and assistants.

In its response to the Department's report, published at the end of last year, UNISON says that although it endorses the broad thrust of the Government's aims in the NHS and pharmacy plans, and the skill mix, paper its concerns "have primarily been on shortcomings in delivering the plan, particularly the inability so far to ensure that there are sufficient numbers of well-managed, well-motivated staff with the right skills in the right place at the right time".

UNISON says that it wants to see skill mix decisions being driven by appropriate

risk assessments with delegation of work to the right members of staff. It is opposed to grade mix decisions driven simply for cost reductions.

"To be successful, the new extended roles must be supported by appropriate training to support staff competence, prior to the adoption of new roles," the union says.

Looking at specific parts of the skill mix paper, the union says that "protocol medicines supply schemes", which would allow suitably qualified pharmacy technicians to hand over dispensed medicines without supervision from a pharmacist, would need careful piloting and adequate resources before they are introduced. It notes that decisions relating to skill mix will need to be made alongside the "Agenda for change" pay discussions.

Independent Pharmacists' Association to be launched in Britain in the spring

THE inaugural meeting of a new Independent Pharmacists' Association is to be held on 6 April. Membership of the association is expected to cost £150 a year.

The association is being set up by Graham Southall-Edwards, a pharmacist and barrister who already has commitments from 50 pharmacists to join and expects to see up to 200 at the launch meeting. The meeting is likely to be held in Andover, Hampshire, or in Coventry.

Mr Southall-Edwards said: "Given the recent news of a flood of European Union and other pharmacists being brought into the United Kingdom by Lloydspharmacy

and the immediate reported effects on locum situations and rates, the balance of power has swung further into the hands of the large corporate employers. There will inevitably be a knock-on effect on employment opportunities and salaries too."

He adds that £150 — about one day's pay — is not too much to pay for such an association when compared with the subscription rates for membership of other professional associations.

Mr Southall-Edwards can be contacted by e-mail (barrister@netway.at) for further information.

NHS Scotland logos sent to pharmacies



Community pharmacies are being encouraged to display the NHS Scotland logo windows

COMMUNITY pharmacies in Scotland have been sent stickers and posters to display bearing the National Health Service in Scotland logo.

A letter to pharmacy contractors signed by Bill Scott, chief pharmaceutical officer at the Scottish Executive, and Frank Owens, chairman of the Scottish Pharmaceutical General Council, notes that encouraging pharmacies to display the NHS Scotland logo was a commitment in the Scottish pharmaceutical care strategy. "We write to commend this initiative to you and to seek your support in displaying the materials in your windows and dispensary areas," the two signatories say.

Mr Owens told *The Journal* that a recent survey by the Scottish Consumer Council (*PJ*, 30 November 2002, p769) found that only half of the respondents believed that community pharmacies were part of the NHS.

Risk of developing diabetes reduced in women with heart disease taking HRT

WOMEN with coronary heart disease who take hormone replacement therapy (HRT) have a substantially reduced risk of developing diabetes, a large randomised controlled trial has shown.

The findings come from the heart and estrogen/progestin replacement study (HERS), which randomised 2,763 postmenopausal women with heart disease to receive HRT or placebo for four years. The active therapy used in the trial was 0.625mg conjugated oestrogen plus 2.5mg medroxyprogesterone acetate. Although the main study end point was prevention of further coronary events, and the incidence of diabetes was not specified as a secondary outcome, blood glucose levels were selected as a possible variable that might influence the effects of HRT on coronary heart disease.

Fasting blood glucose levels were measured at baseline and at the end of the trial. New cases of diabetes were defined as either a fasting glucose level of 6.9mmol/L at year one or the end of the trial, self-reported new

diabetes or the presence of any complication directly related to diabetes.

At the start of the study 718 women had diabetes, 218 had impaired glucose tolerance and 1,811 women were normoglycaemic. Fasting glucose levels rose among women assigned to placebo but did not change among women receiving HRT. Overall, the incidence of diabetes was 6.2 per cent in the 1,380 women assigned to HRT compared with 9.5 per cent in the 1,383 women assigned to placebo, a 35 per cent reduction in the relative risk of diabetes ($P=0.006$).

However, the researchers say that although the observation may provide important clues about the metabolic effects of HRT, the risks and benefits of hormone therapy must be considered for each individual before deciding whether or not the therapy is warranted for prevention of diabetes. "Postmenopausal women at high risk for incident diabetes, such as those with impaired fasting glucose, may benefit from HRT," write the researchers. But they add



HRT may benefit women at high risk of developing diabetes

that this benefit must be weighed against the increase in venous thromboembolism, the early risk of coronary events after starting HRT, and the increased risk of breast cancer associated with long-term use (*Annals of Internal Medicine* 2003;138:1).

Sildenafil effective for sexual dysfunction associated with use of antidepressants

SILDENAFIL (Viagra) is an effective treatment for sexual dysfunction associated with antidepressant use, a study shows. More than half of patients who took sildenafil reported much or very much improved sexual function, compared with less than one in 20 of the patients who took placebo.

Researchers randomised 90 patients (mean age 45 years) with major depression that was in remission to sildenafil 50mg or 100mg, or placebo. Patients were told to take one tablet one hour before they anticipated sexual activity, and to have regular sexual activity throughout the six-week treatment period.

On average, patients had been taking antidepressants for between two and three years, and had between three and four symptoms of sexual dysfunction. A total of 85 per

cent of patients completed assessments during the treatment period and 93 per cent took at least one dose of the study drug.

Of the 44 patients who took sildenafil 24 had much or very much improved sexual function compared with two of the 45 patients who took placebo. Erectile function, arousal, ejaculation, orgasm and overall satisfaction improved among sildenafil-treated patients compared with those taking placebo. Depression scores remained similar in both groups.

The researchers say that this is the first well-designed study to show an effective antidote to sexual dysfunction associated with antidepressant use. But they warn that the results may only relate to men who fulfilled the study protocol criteria and cannot be generalised to women or other groups without further trials (*JAMA* 2003;289:56).

Possible new role for tamoxifen

TAMOXIFEN could be used to stimulate the ovaries of former breast cancer patients who wish to increase their chance of becoming pregnant, say American researchers.

They report a small study in which 12 women who had survived breast cancer received 40–60mg of tamoxifen for around seven days starting on days 2–3 of their menstrual cycle for 15 cycles. These patients produced a greater number of mature eggs than a group of five patients who had previously undergone natural cycle *in vitro* fertilisation (IVF). "Tamoxifen helped a higher proportion of patients to potentially preserve their fertility and attempt pregnancy," they say.

The researchers also report the first occurrence of pregnancy and live birth after tamoxifen stimulation, IVF and embryo transfer (*Human Reproduction* 2003;18:90).

Advertisement

Candesartan could help in preventing migraines

CANDESARTAN (Amias) could prove to be an effective agent for migraine prophylaxis, according to the results of a small placebo-controlled study.

The researchers say that the response rate, lack of side effects and absence of drug interactions mean that the angiotensin II receptor antagonist warrants further study in a larger trial. In all, 60 patients aged 18 to 65 years who suffered between two and six migraine attacks per month were randomised to receive either candesartan 16mg or placebo for 12 weeks after a four-week placebo run-in phase. Then, after a second four-week period on placebo, the two groups had their therapies switched for a further 12 weeks.

The main study end point was number of days with headache. Secondary end points included the number of hours with headache, days when migraine was present, total hours with migraine, severity of headache, disability, number of doses of triptans and analgesics, and acceptability of treatment.

On average patients treated with candesartan had 4.9 fewer days with headache than placebo-treated patients (18.5 vs 13.6, $P=0.001$). Candesartan-treated patients also experienced 36 per cent fewer hours with migraine compared with placebo-treated patients. Headache severity was also reduced among the candesartan group compared with placebo.

Between 32 and 46 per cent of patients responded to candesartan treatment, defined as at least a 50 per cent reduction on at least one of the efficacy outcomes. Although no mode of action for candesartan as a migraine prophylactic has been proven,

the researchers say blocking angiotensin II has several effects relevant to migraine. These include direct vasoconstriction, increased sympathetic discharge and release of adrenal medullary catecholamine.

However, the characteristics of the drug itself "may make it suitable as a migraine prophylactic drug", they write. "In this study the incidence of adverse effects attributable to candesartan was similar to that for placebo, and it has no significant drug interactions," comment the authors.

They add that candesartan does not affect pulse rate and can safely be used in patients with asthma (*JAMA* 2003;289:65).

Call for Schering to repay NHS money over Yasmin claims

THE Consumers' Association has called on Schering Health Care to repay £200,000 to the National Health Service following misleading claims about its oral contraceptive product Yasmin (ethinylestradiol with drospirenone).

Schering was forced to withdraw advertisements for Yasmin at the end of last year after the Medicines Control Agency ruled that they were unacceptable (*Pf*, 14 December 2002, p837). However, the *Drug and Therapeutics Bulletin* said at that time that the MCA had been incompetent because the Prescription Medicines Code of Practice Authority had ruled against the advertisements in September 2002 after complaints published in an article in the *DTB* in August.

Now the Consumers' Association, publisher of the *DTB*, wants Schering to repay £200,000 to the NHS which it says is the difference in cost between prescriptions written for Yasmin and for the next most expensive alternative.

Professor Joe Collier, editor of the *DTB*, said: "There must be some recompense for the NHS when doctors prescribe expensive drugs in good faith as a result of misleading promotional claims. Schering should voluntarily repay the excess expenditure without recourse to the law courts."

A spokeswoman for Schering said that the company continues to support Yasmin and would not consider making any repayment. "Prescribing decisions are made by doctors and patients together," she said. Yasmin had been one of the most studied oral contraceptives before its launch and a large amount of evidence had been gathered and presented to the licensing authorities. Revised advertising is planned.

Pharmaceutical industry promotions criticised

PROMOTIONAL activities of pharmaceutical companies have been criticised in articles published in two leading medical journals, the *BMJ* and *The Lancet*.

The article published in the *BMJ* last week (2003;326:45) accuses pharmaceutical companies of "corporate sponsored creation of a disease" — female sexual dysfunction (FSD).

Ray Moynihan, a journalist with the *Australian Financial Review*, says that the definition and classification of FSD was drawn up at meetings sponsored, run and attended by pharmaceutical companies. A subsequent article in *JAMA* (1999;281:537 and 1174) reported a total prevalence for FSD of 43 per cent. Mr Moynihan says that this is "a figure now widely cited in both the scientific and lay media" despite questions about the definition and the prevalence.

"The potential risk, in a process so heavily sponsored by drug companies, is that the complex social, personal and physi-

cal causes of sexual difficulties — and the range of solutions to them — will be swept away in the rush to diagnose, label and prescribe," Mr Moynihan says.

The article in *The Lancet* last week (2003;361:27) reports an assessment of advertisements carried in six Spanish medical journals in 1997. Researchers from the Fundación Insitituto de Investigación en Servicios de Salud, Valencia, Spain, led by Dr Pilar Villanueva, found 264 different advertisements for antihypertensives and 23 different ones for lipid-lowering drugs in a six-month period. These made a total of 125 referenced claims. Excluding 23 claims with unpublished data, the researchers say that for 45 of the claims (44 per cent) the literature did not support the statement made.

The most frequent reason for claims being unsupported was that the advertisements recommended the use of drug in a patient group different from that studied in the trial. Other problems included transfer-

ring results from high-risk groups to the general patient population, exaggerating trial results or overemphasising their significance, and using animal data to support human use.

The authors say that medicines advertising rules in Spain are covered by the same European directive that applies to the United Kingdom and that extracts from medical journals or scientific papers are required to be truthfully reproduced. They are also critical of the reproduction of images of medical journals such as *The Lancet* in advertisements "to reinforce the credibility of the product".

In an accompanying editorial (*ibid*, p10), Dr Robert Fletcher of Harvard Medical School, Boston, cautions readers not to accept claims made in either advertisements or original research uncritically. "Regulation of advertising claims is not strong or consistent enough to protect readers from misinformation," he says.

Celecoxib as good as diclofenac plus omeprazole in gastric bleeds

CELECOXIB (Celebrex) is as effective as diclofenac plus omeprazole at preventing recurrent bleeds among arthritis patients with a recent history of ulcer bleeding, a randomised controlled trial has shown.

However, the authors of the study warn that neither regimen completely protected against recurrent episodes among patients with a history of bleeding ulcers. They also found that renal toxic effects among high-risk patients taking celecoxib or diclofenac plus omeprazole were common.

In all, 287 arthritis patients who tested negative for *Helicobacter pylori* were randomised to receive 200mg celecoxib twice daily or 75mg extended release diclofenac twice daily plus 20mg omeprazole once daily for six months. Safety and compliance with each regimen were assessed every two months. The main end point of the trial was recurrent ulcer bleeding within the six-month study period.

At six months 4.9 per cent of patients who had received celecoxib suffered recurrent ulcer bleeding compared with 6.4 per cent of patients treated with diclofenac plus omeprazole (seven vs nine patients). Patients' assessments of their arthritis pain did not differ between the two groups. Dis-

continuation rates were similar for both groups, at 13.3 per cent among patients taking celecoxib and 11.9 per cent for patients taking diclofenac plus omeprazole.

Renal adverse events such as hypertension, peripheral oedema and renal failure were common, the authors report. Among patients with renal impairment at the start of the study, half of those receiving celecoxib and 41 per cent of those receiving diclofenac plus omeprazole suffered renal adverse events.

"The substantial proportion of our patients with co-existing medical conditions, such as renal disease, diabetic nephropathy and heart failure, probably accounts for the high incidence of adverse renal events," the study authors write. They add that the renal toxicity of cyclooxygenase (COX) 2 inhibitors is probably similar to non-selective non-steroidal anti-inflammatory drugs.

The researchers call for further studies to see whether a combination of a COX-2 selective inhibitor and proton pump inhibitor can reduce the risk of ulcer complications among patients with multiple risk factors (*New England Journal of Medicine* 2002;347:2104).

Pharmacist supports "women into public life" at Number 10

MADELEINE KEYWORTH, FRPharmS, was one of a number of women invited to a reception hosted by Cherie Blair at 10 Downing Street last month. The event marked the launch of a Department of Trade and Industry guide explaining how women can become more involved in public life.

Mrs Keyworth is chairman of Doncaster and South Humber Healthcare NHS Trust, which provides a range of mental health and other related services to north and east Lincolnshire, Doncaster and Rotherham. She has served on a number of health boards.

In addition to her public duties, Mrs Keyworth works as a locum community pharmacist, a university lecturer and a post-graduate pharmacy tutor.

Last year, Mrs Keyworth chaired a conference in Scunthorpe for the DTI's Women and Equality Unit. Speaking of the new guide, Mrs Keyworth said: "There are lots of women who may already be involved in their community, as school governors for instance, but who do not know how to take the next step. These are the women we want to connect with so that we can help them to realise their full potential."

ROYAL PHARMACEUTICAL SOCIETY NEWS

Branch websites

More than a quarter of the Society's 130 branches now have their own websites (p65).

Practice guidance

The Society has introduced web-based versions of its guidance on pharmacy computer systems and on information protection and security. The guidance will be reviewed continuously and amended as necessary to reflect changes in Government policy and the progress of NHS projects (p65).

PJ Online

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

Pharmacy information pointers

These are articles produced and updated by the Society's Information Centre:

- Identification of foreign medicines
- Technical information service publications
- Medicines requiring storage at low temperature in the pharmacy.

www.pjonline.com/pip

Special interest groups

The Society section of *The Journal* publishes articles and reports from the various

special interest groups (that include community, veterinary, industrial, hospital and academic pharmacists).

www.pjonline.com/sig

Back issues

All of the back issues of the journals on *PJ Online* can be accessed by publication date.

www.pjonline.com/backissues

Advice to patients

This series on commonly used drugs is intended as a reminder of points to be made by pharmacists as they hand out dispensed medicines.

www.pjonline.com/noticeboard/tips

Advertisement

Selective adhesion molecule inhibitor effective in treating Crohn's disease . . .

NATALIZUMAB (Antegren), a selective adhesion molecule inhibitor, increases rates of clinical response and remission in patients with Crohn's disease, researchers report.

Natalizumab, which is being jointly developed by Biogen and Elan for use in Crohn's disease and multiple sclerosis (MS), is a recombinant, humanised monoclonal antibody that binds to α_4 integrin, a specific adhesion molecule, on the surface of immune cells. The companies explain that by binding to α_4 integrin, natalizumab may stop immune cells from leaving the bloodstream and prevent them from migrating into the gastrointestinal tract in Crohn's disease or the brain in MS and making the disease state worse.

Dr Subrata Ghosh, Western General Hospital, Edinburgh, and colleagues assigned 248 patients with moderate to severe Crohn's disease to receive one of four treatment regimens: two infusions of placebo; one infusion of natalizumab 3mg/kg

and one infusion of placebo; two infusions of natalizumab 3mg/kg; or two infusions of natalizumab 6mg/kg. Infusions were given four weeks apart.

The researchers say that although the rate of remission in the group that received two infusions of natalizumab 6mg/kg was not different from the rate in the placebo group after six weeks (primary end point), the remission rate was superior at weeks four and eight. All three natalizumab groups had a higher rate of clinical response at weeks four, six and eight than placebo. The onset of treatment effect was evident as early as two weeks after initiation of treatment and the response rate was sustained for up to eight weeks after the second infusion in patients who received two infusions of natalizumab.

The researchers conclude: "On the basis of our short-term study, the efficacy of natalizumab for reducing signs and symptoms of Crohn's disease appears to be at least similar to that of the tumour necrosis factor a-

inhibitor infliximab." However, they add that the longer term benefit and safety of natalizumab and its value relative to other therapies for Crohn's disease remain to be defined (*New England Journal of Medicine* 2003;348:24).

. . . as well as for the treatment of multiple sclerosis

Patients with relapsing multiple sclerosis (MS) who are treated with natalizumab (Antegren) have fewer inflammatory brain lesions and fewer further episodes over a six-month period than those given placebo, researchers confirm.

In a phase II study of 213 patients at 26 sites in the United Kingdom, United States and Canada, researchers found that relapses occurred in 13 patients treated with natalizumab 3mg/kg (n=68) and 14 patients treated with natalizumab 6mg/kg (n=74), compared with 27 patients in the placebo

group (n=71). Patients were treated every 28 days for six months.

Reductions in the mean number of new lesions in both natalizumab groups were also seen. The percentage of new lesions per patient during the treatment period was 0.7 per cent in the natalizumab 3mg/kg group, 1.1 per cent in the natalizumab 6mg/kg group and 9.6 per cent in the placebo group.

Those in the placebo group reported a slight worsening in wellbeing whereas those in both natalizumab groups reported an

improvement — a finding which should be interpreted with caution, the researchers say.

They comment: "Our results provide evidence of a role of α_4 integrin — and the immune cells that express it — in the pathogenesis of acute inflammatory lesions in patients with multiple sclerosis (*New England Journal of Medicine* 2003;348:15). Phase III trials of natalizumab in MS are under way.

Similar results from this study have been reported previously in *The Journal* (6 October 2001, p456).

Call to abandon body surface area for dosing anticancer drugs

BODY surface area should not be used to determine starting doses of anticancer agents in phase I trials, researchers say. Instead, alternative dosing strategies should be evaluated.

Dr Sharyn Baker, Johns Hopkins University, Baltimore, and colleagues retrospectively assessed the pharmacokinetics of 33 agents tested in phase I trials from 1991 to 2001 as a function of body surface area in 1,650 adults with cancer. Twelve of the drugs were administered orally, 19 intravenously and two by both routes.

Body surface area, the traditional way of determining individualised anticancer drug doses, has previously been thought to reduce interpatient variability to drug exposure and effects. However, the researchers found that, for all but five agents, body surface area-based dosing was not associated with a reduction in interpatient variability in drug clearance. They also found that for the

agents for which clearance was associated with body surface area, only up to a third of the total variability could be explained by differences in body surface area.

The researchers recommend that the practice of calculating starting doses based on body surface area in phase I trials should be abandoned. They say that a fixed total dose is feasible for use in such trials for the development of both cytotoxic and non-cytotoxic targeted anticancer agents and should be calculated on the basis of an average body surface area of 1.86m².

They suggest that to produce more rational dosing schemes for oncology practice dose refinement for novel targeted agents should be based on finding an exposure that produces a biologic or molecular effect on a drug target that is associated with a desired therapeutic outcome or avoidance of a toxicologic outcome. "For cytotoxic agents that have a narrow therapeutic win-

dow, efforts should continue to focus on defining individual doses that are based on patient characteristics that are known to affect drug clearance (eg, age, sex, renal function and use of concomitant medications)."

The study is published in the *Journal of the National Cancer Institute* (2002;94:1883).

BRIEFLY

Dendritic cell vaccine for HIV?

In *Nature Medicine* this month researchers find that dendritic cell vaccines show promise as a means to control diseases caused by immunodeficiency viruses. They report the use of such a vaccine in simian immunodeficiency virus-infected rhesus monkeys (2003;9:27).

Complete remission seen for multiple myeloma with new enzyme inhibitor

COMPLETE remission of advanced stage multiple myeloma can be achieved in patients treated with the proteasome inhibitor bortezomib (Velcade), phase II data show.

Bortezomib, which is being developed by Millennium Pharmaceuticals, may be an effective way of targeting cancer cells while sparing healthy ones (*Pf*, 2 November 2002, p637). Researchers assigned 202 patients with refractory or relapsing multiple myeloma to receive bortezomib 1.3mg/m² body area on days one, four, eight and 11 of a 21-day cycle for up to eight cycles. Before this treatment they had an expected survival time of six to nine months and had previously been treated with an average of six therapeutic regimens.

Of the 193 patients evaluated, complete remission was seen in 4 per cent of patients. This was defined as 100 per cent disappearance in myeloma protein (a marker of tumour burden), negative immunofixation testing (an antibody test for trace amounts of myeloma protein), less than 5 per cent

plasma cells in the bone marrow, no increase in size of or number of lytic bone lesions and disappearance of plasmacytomas. Myeloma protein disappeared completely in an additional 6 per cent of patients but their immunofixation test was positive. The mean survival time was 16.4 months and, overall, 59 per cent of patients responded to treatment or their disease stabilised.

In another phase II trial, researchers investigated bortezomib in 54 patients with early stage multiple myeloma who had relapsed after previous first-line treatment. Patients were randomised to receive bortezomib 1mg/m² or 1.3mg/m² body area for up to eight cycles. Those not responding to treatment after two or four cycles were additionally treated with dexamethasone.

Overall, 59 per cent of patients treated with bortezomib 1mg/m² (n=27) and 69 per cent of those treated with bortezomib 1.3mg/m² (n=26) responded to treatment or their disease stabilised. Complete remission was achieved in 4 per cent of each treatment

group. Adding dexamethasone increased the overall response rate in both groups.

Data were presented at the 44th annual meeting of the American Society of Hematology held in Philadelphia last month.

New drug for treating malaria

FOSMIDOMYCIN, a phosphonic acid derivative, is a safe and effective treatment for uncomplicated malaria in adults, researchers say.

Fosmidomycin has been shown, *in vitro*, to suppress the growth of multi-resistant strains of *Plasmodium falciparum*. Researchers assessed the tolerability of fosmidomycin 1.2g, given orally every eight hours, in 27 adults with signs and symptoms of *P falciparum* malaria. Nine of them were treated for five days, eight for four days and 10 for three days.

They found that by day 14, 89 per cent of those treated for five days, 88 per cent of those treated for four days and 60 per cent of those treated for three days were cured. Symptoms, such as fever, rapidly resolved. Although parasitaemia reoccurred in one patient in each of the five-day and four-day treatment groups and in four patients in the three-day group, parasite clearance was rapid and did not differ between the groups. An increase in the proportion of gametocyte carriers was observed on day 14 compared with that at the start of treatment, which, the researchers say, is a worry because of the potential risk of enhanced transmission.

However, the researchers comment that the data should be interpreted with caution as the study involved a small number of patients (*Lancet* 2002;360:1941).

Ximelagatran reduces VTE risk

XIMELAGATRAN (Exanta), a direct thrombin inhibitor, reduces the risk of recurrent venous thromboembolism (VTE) by 84 per cent over 18 months compared with placebo, new data show.

At the 44th meeting of the American Society of Hematology, held in Philadelphia last month, researchers revealed the benefit of treatment with ximelagatran over an extended period and the prolonged risk of recurrence of VTE seen in patients given placebo.

In the thrombin inhibitor in venous embolism (THRIVE III) study, 1,233 patients who had been treated for six months with warfarin after suffering an initial VTE were randomised to receive either ximelagatran or placebo for 18 months. The researchers found that 12 of the 612 patients treated with ximelagatran 24mg twice daily suffered a further VTE by the end of the study, compared with 71 of the 611 patients in the placebo group — a relative risk reduction with ximelagatran of 84 per cent ($P<0.0001$).

Ximelagatran was also found to be associated with a similar incidence of major and minor bleeding to that with placebo (estimated cumulative risk 23.9 per cent vs 21 per cent, $P=0.1703$), suggesting that the new antithrombotic is free from the increased risk of bleeding seen with prolonged use of anticoagulants currently used in clinical practice.

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