

# P The Pharmaceutical Journal

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## BPC 2009

This supplement to *The Pharmaceutical Journal* covers many of the sessions from BPC 2009, held in Manchester from 6 to 9 September. It completes the coverage of the conference published in *The Journal* on 12 September

## Practice

In an article based on his address to the conference, this year's Practice Chairman discusses the nature of practice research and the challenges faced in sustaining it. There are also sessions on innovation, remote supervision, medicines use reviews, and specialist and advanced practice

## Science

In addition to the Science Chairman's address and science abstracts, the supplement covers a number of sessions related to innovations in discovery, delivery and diagnostics for cancer, infectious diseases and diabetes

## BPCTV

This supplement is accompanied by a DVD that gives a contrasting flavour of what happened at the conference

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**BPC 2009:  
covering science  
and practice**

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# Innovation is the key

This year's British Pharmaceutical Conference — once again held in Manchester — was something of an innovation. It was divided into two, with the practice sessions starting on Sunday 6 September and the science sessions beginning the day after.

Innovation was also the underlying theme running through the two parts: the practice sessions were entitled "Quality and safety: old values, new vision"; and the science sessions "Technologies for healthcare: from laboratory to practice."

## Greater imperative for pharmacists to play their part in ensuring that scarce resources are used wisely and effectively

Practice, almost by definition, is about the here and now — how pharmacists care for their patients, what lessons can be learnt from leading edge practitioners that can be integrated into normal activities. Science, on the other hand, is more about the future — what today's developments and breakthroughs will do for patient care tomorrow.

With the expectation that the NHS will face some years of austerity from 2011 following the banking crisis

of 2008, there is an even greater imperative for pharmacists to play their part in ensuring that scarce resources are used wisely and effectively. The Department of Health has come up with an acronym to define how the NHS should be tackling service reform in financially challenging times. QIPP — quality, innovation, productivity and prevention are the drivers underlying new activity in healthcare.

The chief pharmaceutical officer for England, Keith Ridge, said that the safe and cost-effective use of medicines will feature prominently in the coming years under QIPP (pB10). And a QIPP project in secondary and tertiary care is being led by Martin Stephens, national director for hospital pharmacy in England, who outlined the approach in another session (pB19).

This was echoed by Jeremy Savage, deputy chief pharmaceutical adviser to the Welsh Assembly Government. He pointed out that judicious use of automation and new technology in hospitals in Wales has reduced dispensing errors and improved the efficient use of the workforce (pB11). In another session the benefits of remote supervision in Canada were described (pB12), which may have lessons for the future in the UK.

Dr Ridge also acknowledged the part that the pharmaceutical industry will play in helping the UK economy recover as new medicines come to market. Although the days of the massive blockbuster may be over, and the industry faces an uncertain short-term future (pB29), speakers also emphasised how important innovation is in protecting pharmaceutical revenues in order to ensure research and development can flourish (pB31).

The conference also covered many examples of drug development in oncology, anti-infectives and diabetes — all clinical areas where significant progress has been made in recent times and where innovation must continue if the health needs of Britain are to be met.

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# Society's President urges profession to unite to create a brighter future

In his address to BPC 2009, the Royal Pharmaceutical Society's President, **Steve Churton**, described recent initiatives that demonstrate how the Society has become more member-focused and spoke of the new professional body's "commitment to pharmacy"

This is a historic conference for us — the last one with the Royal Pharmaceutical Society as joint regulator and professional body. The last one of a long and proud line of conferences that have marked the milestones and celebrated the high points in our profession.

As we take this opportunity to realign ourselves, it is right that we recognise and pay tribute to our founding fathers, and those who followed in their footsteps, to build upon their vision.

It is also right that we learn from their experiences and I genuinely believe that we have the responsibility and the ability to leave as our legacy a body fit to lead a modern, progressive and respected profession, which future generations will thank us for.

It is an undisputed fact that pharmacy is regarded by millions of people, patients or otherwise, as a fundamental component of effective healthcare delivery. It is also undisputed that we are now on the brink of achieving arguably the most significant change in our profession in nearly 170 years.

## Initiatives

There are numerous examples of initiatives we have embarked upon during the year that demonstrate, without doubt, that the Society has a purpose far beyond the regulatory role, which many see as our overriding focus.

Working with other pharmacy bodies to grasp the opportunities presented in the pharmacy White Paper for England, seizing the patient safety agenda, launching the workplace pressures initiative and leading the campaign to decriminalise dispensing errors. These are just some of the initiatives we can proudly point to.

When I was elected President last year, I knew that the issue of workplace pressures was one I wanted to tackle and in January I launched our campaign. The campaign has been successful in raising the profile of what many of us experience but perhaps do not have the confidence or opportunity to speak out about effectively. You have told us that the increasing number of prescriptions, the lack of rest breaks, not being able to delegate effectively, feeling unsupported to deliver extended services, unrealistic targets, long working hours and burdensome paperwork all contribute to a more stressful working environment.

We are now leading the debate on these issues and this coming year will see progress made with many of them. We have a programme of work stretching ahead of us, to



**Steve Churton: no representation means no influence**

work in partnership with those who can bring about the improvements and solutions we are all looking for.

We have also taken the highly unusual and significant step of issuing a formal Council statement [about rest breaks] to the profession (*PJ*, 5 September, p229). Such statements are reserved for issues where we wish the profession to take immediate action.

## Decriminalising dispensing errors

Standing here last year I know it did not cross my mind that we would see the prosecution of a pharmacist for making a human error. A genuine dispensing error — yet defined by legislation, laid too long ago, as a criminal offence — and one which quite understandably outraged the profession.

We responded quickly and robustly, resolving to campaign vigorously to stop the

continuing criminalisation of dispensing errors. We campaigned hard, and engaged with the profession to lobby MPs and senior political figures. We — the profession as a whole — captured political hearts and minds across all parties, and we won the debate in Parliament and in Whitehall.

We have had outstanding parliamentary success. The Early Day Motion has been signed by over 220 MPs, which places it in the top 1 per cent of EDMs this year — a fantastic response by any standard and one that I would like to sincerely thank the profession for getting behind.

In time the law will be amended and, as we continue to work to deliver this permanent change, we will strive to raise the profile of this in the mind of every pharmacist, to ensure that he or she does not fall foul of the current legislation. In the meantime, active discussions are now under way with the Department of Health, the Medicines and Healthcare products Regulatory Agency and the Crown Prosecution Service.

We have instigated and participated in many discussions with the main political parties, building relationships with key decision-makers and influencing those in a position to influence policy and legislation in England, Scotland and Wales.

This is only the start. We will continue to develop our relationships with policy-makers to promote your views, interests and concerns.

We have also had another hugely successful year in the media, shaping public awareness of the services and expertise we offer, and reinforcing positive perceptions of the value we contribute.

## Charter changes

The proposed Charter changes, and the encouraging vote in favour [of them], were a major milestone for the profession during the year. You told us that it is important for us to keep our Royal Charter but that changes to enable a more relevant, progressive, efficient, inclusive, supportive and representative organisation should be made.

The changes you voted for mean that we now have the prospect of a different organisation to the one you have been used to. The work of the new body will be largely devolved to the national pharmacy boards in the three countries, with policy-making, representation and professional leadership all taking place where they should be — closer to members, closer to those who can be

Craig Strong



Craig Strong

Steve Churton, Society Chief Executive and Registrar Jeremy Holmes and shadow health minister Andrew Lansley

influenced to shape the pharmacy agenda and closer to those who are better placed to provide the local support that our people need.

The boards will take a far more substantial role, enabling us to engage more effectively with the devolved administrations, and to recognise and influence the increasingly diverse national healthcare programmes. The central assembly will play an important role as well, providing the necessary strategic direction, financial management and appropriate degree of overarching governance for the new organisation.

The changes to the Charter also remove all references to regulation to set free this organisation so that it can be truly independent from the Government and focus on supporting the interests of members — so you can achieve your professional ambitions and be the very best you can.

Throughout the year we have been working hard through the Pharmacy Regulation and Leadership Oversight Group — the group brought together to oversee the establishment of the new regulator, the General Pharmaceutical Council — and directly with the Department of Health, to ensure that the transition goes smoothly.

I regard regulation as a privilege. It bestows trust and confidence in the profession and the Society's track record as the profession's regulator has again been acknowledged by the Council for Healthcare Regulatory Excellence. Next year, when the General Pharmaceutical Council opens its doors for business, when it starts to maintain the register of pharmacists, technicians and premises, it will act in the public interest. It will establish and promote standards and requirements for pharmacy owners, superintendent pharmacists and premises. It will be concerned with proficiency, conduct, ethics and performance, and it will require all registrants to demonstrate evidence of continuing professional development.

These activities are hugely important for us all, and your professional leadership body will play a crucial role in advising and influ-

encing the regulator, and in supporting and inspiring members to achieve the standards laid down.

### Improved communication

You have told us that this year has seen a marked improvement in the way we have communicated with you. You have said that you now feel more informed about what is happening in the profession and engaged in meaningful conversations with the Council, the national pharmacy boards and the people who support us in London and in our national offices. You have also said that you feel more listened to and that we are now more responsive to your needs.

We have had to make some really tough decisions this year. The debate around the restricted title that led to a Special General Meeting, the changes to the Royal Charter, the calls to delay the implementation of the responsible pharmacist regulations — these were all issues where we had to make decisions that we believe to be right for the profession, even if unpopular with some members.

I ask the profession to reflect on our collective record of achievement. Are we now more member-focused, genuinely seeking to understand what you want and need from us? Have we acted with integrity in a straightforward, transparent and principled manner? Have we demonstrated courage and conviction, often in the face of adversity?

### Being a professional

I believe that being a professional is about focusing on our patients, putting their safety, health and well-being first and foremost. [Among other things] it means using our professional judgement to deliver excellent care and working within a relevant and modern code of ethics and a shared value system. It means not shirking those tough decisions that we are all required to make from time to time. It means being brave, standing up for what you know to be right in the interests of your patients, and knowing when it is right to make a stand.

It involves doing the best you possibly can, taking responsibility to keep your practice and knowledge up to date, showing a commitment to both personal and professional development.

For me, being a professional is also about collaborating with others, within and across sectors of our own profession, as well as promoting strong and effective relationships with colleagues in other healthcare professions.

As a professional, I value excellence in academia and recognise the benefits of developing pharmacy specialists. I also value the role of science and original research, and how this can be most effectively translated into practice in the shortest possible time, for the benefit of patients.

As busy professionals we all know it is not easy to live up to these ideals, to always deliver excellent care, to stay up to date, to take those hard decisions, to extend our practice, to meet with fellow professionals and share ideas. We all need support to be professionals in a modern and rapidly changing world, and a modern and rapidly changing profession.

The more I think about this, the more I talk to others, the more I see what the future could look like if we join together — and what it might be like if we do not — the more I genuinely and passionately believe that all of this can only be delivered by a strong leadership body.

There surely cannot be anyone who seriously thinks we can do all of this — let alone survive as a profession — without the effective, representative and inclusive professional body we are building.

In bringing about the necessary changes we consulted you. I have sensed a feeling among some that we should just “get on with things”. But it is not quite that easy of course. We are facing a period of austerity within healthcare and we will need to fight our corner to achieve our ambitions, especially the services and opportunities laid out in the pharmacy White Paper [for England]. We will need to continue the fight to achieve parity with other healthcare professionals and to

take control of the public debate, raising issues of concern to us as a profession and to them as patients.

It is vital that your new body receives your support. Without it, pharmacy as a whole would lack an authoritative voice when major decisions are being made. No representation means no influence. The profession could well retreat to a position of submission and compliance, passive to the changes imposed upon it.

### Commitment to pharmacy

Over the past few months you will have seen [the “commitment to pharmacy”] branding appearing in many of our communications. Quite simply, we wanted to highlight to you what we really care about. The words, and the meaning behind them, were chosen carefully.

I recognise that “commitment” is a big word. It is more than just a promise, it is a dedication, an assurance, an obligation. It should be considered a strong signal of our intent to change, to demonstrate an unwavering commitment to you and to the profession.

Now I do not think many would argue with the commitments [the professional body is making to the profession] (*PJ*, 12 September, p259 and p272) but I do think we need to deliver on these in a tangible and measurable way. I fully understand that members will want to see evidence of delivery.

We are currently finalising the next wave of deliverables during the 100 days immediately before the “go live” date [for the commitments]. We will continue to listen, plan, resource and deliver. We will continue to be as faithful as possible to the original prospectus and we will continue to recognise the need to nurture and support your new professional body as it comes into being.

The shape, feel and personality of the new organisation is becoming clearer. It is rightly developing from within its own membership. This is exactly how it should be and I applaud all who have been so actively involved and given so freely of their time to benefit the profession, and all of us who are so privileged to be part of it.

Thousands of pharmacists are now beginning to realise the implications and opportunities before us. Those actively supporting this process are not asking what the Society can do for them, they are asking what they can do for the Society.

How refreshing it is to know that there are those who recognise the importance of this venture. How inspirational it is to see the passion on the faces of so many involved. How satisfying it is to hear so many speak in favour of what we are collectively trying to achieve.

Trust is a precious commodity, which is hard to define, harder to win and all too easy to lose. Without mutual respect and trust we are nothing.

During the course of the year I have met with many pharmacists. Not all, it has to be said, speak with affection of the Society and I understand the reasons for this. But it seems



Craig Strong

### Commitment to pharmacy: evidence of delivery needed

to me that there is far more which binds and unites us than there is which divides us.

Together we can be strong. You only need to look at the successful decriminalisation campaign — the result of a groundswell of support from members, and effective and decisive leadership from many quarters — to see that. A lack of trust inevitably leads to fragmentation and weakness, and we simply cannot afford to let this happen at this important time.

The Charter vote is now behind us and you have given us a mandate for change. My thanks to those of you who voted “yes”, for understanding the importance of the changes we proposed and for trusting us to deliver on our commitments. It is clear to me that those who voted “no” also care deeply about the future of our professional body. To those who have since said to me “I didn’t particularly agree with your proposals but I am still joining the professional body”, I say “welcome”.

And to those pharmacists who did not vote at all — those who have yet to find the time or energy to engage with these changes — I understand the pressures you face. I understand that debates about Charters and new bodies can all seem dry and remote from your daily life. But I urge you to get involved because this professional body will be your professional body and will be there to support and help you. We need you to help shape it so

that it meets your needs and gives you what you want.

We are now less than 150 working days away from the planned launch date and I ask everyone in the profession to trust and to support me, and to work with me through these momentous changes.

Our new professional body will be stronger than any single-interest body and will speak with one voice for the whole profession. Our new professional body will empower and enable. It will ensure that each and every pharmacist can truly fulfil their potential and realise their ambition. It will support their professional development and it will shape the environment in which they can flourish and succeed.

I believe that a body which speaks up for pharmacy, a body which is truly representative of the collective will of its membership, and a body which acts with conviction and integrity, will thrive and will be powerfully influential in carving out the future that we all wish to see for our profession.

### Brighter future

We can have a brighter future and it is up to us to make it happen. No one else is going to do this for us. We are limited only by our imagination and our energy. So please use yours and join me today in creating something special — a profession for the future, a future for our profession.

# Practice Chairman's address: why research pharmacy practice?

Drawing on his own research over the past 15 years, BPC Practice Chairman **Peter Noyce** discusses the nature of pharmacy practice research, the insights it provides, its impact and the challenges faced in terms of its capacity and sustainability

The Nuffield Committee of Inquiry on Pharmacy identified the need for practice research in pharmacy, and to develop an academic discipline in the subject nearly 25 years ago. Geoffrey Booth, a former president of the Royal Pharmaceutical Society, was appointed the first professor of pharmacy practice — at the University of Bradford — in the late 1980s.

Despite this, pharmacy at large has relatively little awareness of practice research or its purpose. Responses from “practising” pharmacists to practice research findings range from the prosaic, “Isn’t this a statement of the bleeding obvious?” through the ironic, “Why do you need to know all that detail?” to the surprised, “Didn’t know that was being researched, actually that’s quite useful”.

Much in the way that some of the leading world-class universities have recognised the need to create chairmen in the public understanding of science, I, as the 2009 Practice

Chairman of the British Pharmaceutical Conference, have taken as my challenge raising the awareness and understanding of practice research within pharmacy.

As a basis I draw upon 15 years of research on community pharmacy within the drug usage and pharmacy practice group at the School of Pharmacy and Pharmaceutical Sciences, University of Manchester, to illustrate the range of studies undertaken, the insights they provide and their impact. I have also attempted to outline the contemporary scope of pharmacy practice research, convey its responsive and dynamic nature and reveal its vulnerability.

## Addressing the criticisms of *Which?*

Our early studies were prompted by the repeated adverse criticism of advice-giving in community pharmacies by *Which?* magazine, based on various consumer exercises undertaken by the Consumers’ Association. Although previously a variety of studies had reported on advice-giving<sup>1</sup> they did not provide a definitive response on whether it was inadequate or otherwise inappropriate.

The great strength of including investigators from social science backgrounds in pharmacy practice research groups became apparent at this time. They were familiar, for example, with observational methods and so a series of revealing studies was instigated involving week or part-week long observations in a range of community pharmacies.

What became clear was that there was considerable variation between community pharmacies in responding to symptoms,<sup>2</sup> requests for over-the-counter medicines,<sup>3</sup> referral to other health professionals<sup>4</sup> and whether customers were seen by a pharmacist or a medicines counter assistant. The participating pharmacists also confessed that they were unaware of how their advice-giving routines, including referrals, compared with others, and were keen to reflect on the anonymised results of the studies to benchmark their own service level.

Another parallel study captured the essential nature of advice-giving in community pharmacy<sup>5</sup> (see Panel 1) and demonstrated common mismatches between patient priorities in seeking advice, and the advice given.

Following these findings, the Royal Pharmaceutical Society introduced standard operating procedures to cover advice-giving and required medicines counter assistants to undergo training to support OTC recommendations and sales.

What is striking to the impartial observer is how differently community pharmacies deal with prescription and non-prescription medicines. Yet to many patients it is the cost of medicines to them that is their main interest or concern.<sup>6</sup> From our studies we realised how pivotal this was in determining whether a patient purchased an OTC medicine or sought a GP’s prescription for the product.<sup>7,8</sup> Therefore we postulated that if we could arrange for those patients who were exempt from prescription charges to have non-prescription medicines supplied free of charge under the NHS directly from pharmacies then the management of minor ailments could be transferred from GPs to pharmacists.

The feasibility of this intervention was tested in what was known as the “Care at the chemist” scheme (details of which appear in Panel 2). With findings published in both the *British Medical Journal*<sup>9</sup> and *The Pharmaceutical Journal*<sup>10</sup> in 2001, the framework and evidence base for minor ailments schemes were created. By 2006, over 2,000 pharmacists (one in five) in England were participating in minor ailment schemes as an NHS enhanced service. By 2007, the minor ailments service was introduced nationally in Scotland as an NHS pharmaceutical service.

## Insights into the 2005 contract

A comprehensive description of the implementation of the new community pharmacy contract in England, based on a national survey of primary care trusts, was published in *The Pharmaceutical Journal* in 2006.<sup>11–14</sup>

### Panel 1: Advice-giving in community pharmacy

“... consumer-led, with pharmacy staff mostly responding to customer requests for named products.”

“... characterised by its didactic nature, the emphasis being on checking, instruction and information, at the expense of explanation ...”

“Pharmacy staff are aware of the potential danger of medicines and their prime concern is safety ... consumers appear to be interested in the effectiveness of products.”

Hassell K et al. *Journal of Health Services Research and Policy* 1998;3:219–25

## Practice Chairman

Peter Noyce is professor of pharmacy practice and director of The Workforce Academy at the University of Manchester. He was appointed chairman in pharmacy practice at the university in 1991 and founded the drug usage and pharmacy practice group. He has now been appointed by ministers as professional adviser for the establishment of the General Pharmaceutical Council.

Professor Noyce has a general interest in health services research applied to medicines and pharmacy and is particularly interested in improving the use of resources and reducing the risks within healthcare systems. His major interest is in community pharmacy, both informing and evaluating policy. Recent work has focused on gaining insights into the factors that determine the contribution of community pharmacy to primary and self-care, the commissioning of NHS pharmaceutical services and improving understanding of the culture within community pharmacies.

Current activity in The Workforce Academy is aimed at the development of quality indicators and strengthening the safety of processes and systems. The academy is also looking to develop a programme of work to inform the debate on “fitness to practise” within pharmacy and its assessment, and underpin the modernisation of regulation of pharmacists and pharmacy technicians, and the establishment of the GPhC.

Using this information as a baseline we have now begun to explore particular features of NHS pharmacy services to chart their evolution and assess their impact. A mixed-methods study of medicines use reviews (MURs) revealed a marked difference in the level of engagement between independents and multiples.<sup>15</sup> It also identified several unintended outcomes of the introduction of MURs, including indications of a mismatch between service provision and patient need, adverse responses from GPs compounded by poor communication and unacceptable pressure to maximise MUR volumes by some multiple employers.

There is now a concerted campaign by NHS and pharmacy bodies nationally to improve the quality and targeting of MURs.

A recent study of the impact of the relaxation of control-of-entry regulations in England<sup>16</sup> has revealed that the opening of new NHS pharmacies is concentrated in a minority of PCTs, commonly within 500 metres of other pharmacies. Approximately two-thirds of the new pharmacies are opening under the 100-hour exemption, with nearly 40 per cent being opened by three of the largest supermarket chains. This relaxation of the criteria for awarding new NHS contracts will have a particular impact on the distribution of NHS pharmaceutical services and demand for pharmacists in the north west, where the number of new in-store supermarket pharmacies is double that in London.

(A comprehensive review of the development of policy and practice in community pharmacy in the UK and how this has been informed by practice research has recently been published for an international audience<sup>17</sup>).

### The nature of practice research

At its core, pharmacy practice research comprises the study of pharmacy practice and medicines use. In studying pharmacy practice, the organisation, setting and culture of practice is important. Equally important is an understanding of the interplay between the nature of pharmacy practice and the practitioners themselves. For example, the perspectives and attitudes of the following



Peter Noyce addresses the British Pharmaceutical Conference 2009

pharmacists towards workload, financial rewards, practice innovation, and quality of patient experience are likely to vary: an independent owner planning to sell his pharmacy within the next two years; a mother of young children working as an independent pharmacist prescribing part-time in residential homes; and a newly qualified pharmacist

working shifts in a 100-hour supermarket pharmacy.

The dynamics and influences on pharmacy practice are pivotal in determining service quality and innovation, and patient safety (minimisation of errors). Therefore, an understanding of these is important to pharmacy employers, PCT commissioners, government health departments, and the new General Pharmaceutical Council and professional body.

As the benefits of having an evidence base are gradually being recognised in pharmacy practice itself, the horizon of pharmacy practice research is extending. The need to understand learning and motivation of pharmacists and pharmacy technicians, and to assess their competence and fitness to practise effectively and appropriately, becomes a priority with the modernisation of professional regulation.

Prescribing and medicines management are established research workstreams which pharmacy has often shared with health economics and clinical pharmacology. Now, with the emergence of pharmacist prescribers —

### Panel 2: "Care at the chemist" scheme

**Intervention:** Provide patients exempt from prescription charges with non-prescription medicines under the NHS (for 12 defined conditions) directly from community pharmacies

**Period of intervention:** Six months

**Setting:** One general practice serving approximately 10,000 patients and eight community pharmacies (93 per cent prescription items exempt from charges)

**Results:** For GPs, the number of consultations for acute, minor ailments per 1,000 population per week fell from 6.3 at baseline to 3.9 during the intervention. For community pharmacists, it rose from 8.0 at baseline to 10.4 during the intervention.

The total number of consultations with community pharmacists during the intervention was 576 (37.8 per cent transfer from GPs). Reconsultation rates for the same condition within 14 days were not significantly different between community pharmacists and GPs.

Hassell K et al. *British Medical Journal* 2001;323:146–7

within the wider development of non-medical prescribing — new collaborations are being created with nursing researchers.

### Medicines use

There are two main focuses to research on medicines use: medicines and patients. Pharmacoepidemiology, comprising population-based studies of medicines, and pharmacovigilance, involving the identity and prevalence of adverse drug reactions, have interested a cadre of pharmacy researchers, often working in groups led by clinical pharmacologists.

With the priority on patient safety, pharmacy researchers have extended their interests from the risks of medicines themselves to the risks of medication systems — the prescribing and dispensing and administration of medicines. The focus is on preventable drug-related morbidity, particularly the study of the nature, prevalence and causality of adverse drug events, so enhancing the understanding of medicines-related errors and underpinning the development and evaluation of strategies for error reduction. These investigations involve pharmacists working with occupational and organisational psychologists and applying systems-based approaches from the “high-risk” oil and gas, airline and railway industries to improve medicines safety.

Undoubtedly a major factor affecting patient benefit and safety from prescribed medicines is patient non-adherence. Although an everyday phenomenon, it has a multifactorial cause, and requires empathetic and resourceful pharmacists working in partnership with willing and persistent patients to manage successfully. Pharmacy practice researchers, using techniques and approaches borrowed from health psychology, have made great strides in understanding patients' beliefs about medicines and the nature and causes of non-adherence, particularly in long-term conditions. Now the challenge is to develop validated smart interventions that can be readily applied in routine practice.

### Challenges for practice research

Essentially, these are two types of challenges for pharmacy practice research:

- Awareness and use of practice research
- Succour and sustainment of practice research

The drivers for academic research are impact of outputs, mainly academic and professional articles, and securing competitive funding. Impact depends on methodological rigour and often originality. Within the academic community impact is characterised by publications in peer-reviewed journals with a high bibliometric impact and an impressive citation level. Within health services research, “soft” indicators of research quality include the impact on policy and practice at a national or international level. Health services research funding sources also usually demand a demonstration of relevance, achievability

and applicability of proposed research projects and programmes, and a commitment to effective dissemination of the findings.

In reality, once a research team has reported to the funder and secured publication in a reputable journal, it sees its commitment as essentially complete and the focus moves to raising funds for the next project or programme. It is therefore important that the new professional body bridges the gap between generation and application of research findings to pharmacy practice and policy.

A considerable body of pharmacy practice research has been produced over the past 15 years, with over 880 outputs from the Manchester group alone, including 49 reports on commissioned research. Pharmacy practitioners and policy makers generally have yet to recognise and make best use of the growing evidence base in pharmacy practice.

Creating and developing a new academic discipline within pharmacy has been exciting, but remains immensely challenging. While unique in its focus and pharmaceutical oversight, pharmacy practice research is essentially the application of health services research to pharmacy and medicines.

Health services research is well established as a multidisciplinary activity in leading health or medical faculties with particular strengths in primary care, public health, general medical practice and nursing. Pharmacy practice research has had a particular advantage in settings where it has been able to draw on the expertise and resources of a wider health services research and clinical research environment. Now it is beginning to be recognised as making a valued and unique contribution to informing health care policy, management and practice more widely.

The landscape of pharmacy practice research is now fairly well defined. It is sustained by an appreciation of the pharmaceutical sciences and an understanding of the clinical use of medicines, and the organisation and delivery of pharmaceutical services. It also relies heavily on the application to healthcare of the population-based sciences of psychology, sociology and economics.

What is currently lacking is capacity and, at risk, sustainability. Practice academics generally have heavy teaching loads and so their capacity for research is limited. There are no dedicated funding streams for developing research capacity through doctoral and post doctoral fellowships or sustaining research careers in pharmacy, as there are for medicine, dentistry and nursing. It is not surprising, therefore, the continued supply of senior research-active practice academic staff depends on a handful of schools of pharmacy.

The absence of funding streams for pharmacy-related practice research through government health departments, and the cessation of a programme of commissioned research through the Pharmacy Practice Research Trust, means that the capacity and skill base of the pharmacy research workforce will shrink even further. Without a cadre of

pharmacy researchers with diverse methodological skills, practice research will become less responsive and the evidence base for pharmacy depleted.

Pharmacy practice research like any other endeavour — such as wealth-creation, manufacturing or healthcare — requires investment.

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# Five principles of effective regulation

Gareth Malson and Francesca Rivers report on the new regulatory framework and on the work of the Practice Research Conference Award winner

Bob Nicholls, chairman designate of the General Pharmaceutical Council, shared five principles that he intends to bring to his new role.

The first is that independence of the regulator and the full contribution of lay members are of critical importance when establishing trust and confidence in professional regulation. Independence is assured by appointing council members who are free from the obligation to represent any particular interests, and by appointing equal numbers of lay and registrant members, he said. The latter would allow regulation to be seen to be a partnership between the public and profession.

"Of course, real engagement with the profession and other stakeholders could never be achieved simply through the composition of a council of 14," said Mr Nicholls. "It is much more about genuine outreach and engagement, and the GPhC will make this a priority."

Secondly, effective regulation is about working in partnership with the professions, he said. "Partnership working clearly starts with the people who are appointed to the council and statutory and non-statutory committees working effectively together," explained Mr Nicholls. "But, importantly, it also means making sure there is a wide variety of trusted mechanisms through which we can listen to and genuinely involve professionals."

Thirdly, effective regulation is about listening to and involving patients and the public.



Bob Nicholls: engagement a priority

"The new council will be endeavouring to get inputs from patients and the public, and their representative organisations, in all its work," said Mr Nicholls.

Fourthly, regulation must be proportionate. "I know many professionals fear the so-called burden of regulation," said Mr Nicholls. "Proportionate means regulation must be fair but not over-burdensome. While too little regulation or professional dominance is clearly not an option, we must avoid duplication and the cost of regulation must be reasonable."

"All aspects of regulation should deliver clear benefits to the public. This will be a challenge to the new council and I'm sure we'll be able to rely on many of you to point out if you think we are letting regulation become disproportionate."

Finally, regulation should be about working to sustain and improve standards and the quality of services, rather than simply disciplining or punishing poor practice, he said.

"Standards will help professionals develop the knowledge and skills they need to build rewarding careers, and provide a clear framework for innovation and improvement," he explained. "The key issue, I believe, is about using standards to create a culture of learning — so that where there is poor practice or behaviour, we seek to learn from it rather than simply punish the individual."

"I hope you will agree this is a worthwhile aspiration for the whole profession, and one in which we can work together."

He announced that the formal consultation on the draft standards for the GPhC was due to be launched later this year, but also that they will be available for early comment until 18 September on the GPhC website ([www.pharmacyregulation.com](http://www.pharmacyregulation.com)).

He concluded: "Clearly pharmacists have been regulated well and effectively by the Royal Pharmaceutical Society. It is my intention that the GPhC builds on this excellent tradition as a foundation for its work."

## Assessing risk within pharmacy practice

Many of the risks faced by patients in hospitals and community pharmacies are preventable, and could be averted by the use of targeted interventions, said Darren Ashcroft, director at the Centre for Innovation in Practice, Manchester School of Pharmacy and Pharmaceutical Sciences.

Dr Ashcroft spoke to the conference after accepting the Practice Research Conference Award at the British Pharmaceutical Conference for his research into medicines use and safety. Often medication problems are not pharmacological, but stem from issues such as wrong diagnosis, prescription of the wrong drug or incorrect drug administration — which represent failures in the medicines management system, he said.

In an early study examining 60,525 prescription items dispensed from 34 pharmacies, Dr Ashcroft revealed that 0.71 per cent of dispensed items required pharmacist interventions — with 10.7 per cent of these interventions averting potentially serious prescribing errors.

He followed this up with an examination of dispensing error rates via a prospective

study involving 35 community pharmacies and 125,395 dispensed prescription items. An overall dispensing error rate of 26.3 errors per 10,000 items dispensed (95 per cent confidence interval 23.6–29.3) was discovered, with errors mainly caused by the misreading of a prescription or similarity of medicine names or packaging. Dr Ashcroft's research showed that distractions and excessive workload were associated with 34.5 per cent of the dispensing errors, with staffing issues at play in 25.9 per cent of cases.

Dr Ashcroft has developed a number of tools based on his research, including the Manchester Patient Safety Assessment Framework (MaPSAF), developed in conjunction with community pharmacists and backed by the National Patient Safety Agency. The framework is designed to bring the concept of safety culture to community pharmacies and is available from the Manchester university school of pharmacy website ([www.pharmacy.manchester.ac.uk](http://www.pharmacy.manchester.ac.uk)).

Dr Ashcroft has also developed a Pharmacy Safety Climate Questionnaire (PSCQ) to survey staff attitudes towards

safety. Responses from 998 community pharmacies in the UK have revealed that 29 per cent of staff believe patient safety incidents in the pharmacy tend to recur. Nearly 40 per cent of respondents (39 per cent) reported an insufficient number of staff to handle the workload, with a quarter reporting longer working hours than are sensible for patient care. Tensions between staff members were also noted by nearly a quarter of respondents (24 per cent). Locum pharmacists and national chains scored lower safety ratings than pharmacy owners and employees, or independent pharmacies and small or local chains.

The study is currently being extended to the US and the questionnaire is being translated in order for it to be used in five countries across Europe.

Dr Ashcroft has also recently secured funding from the Royal Pharmaceutical Society to undertake a detailed assessment of risk within pharmacy practice. "It is intended that these results will start to underpin the development of revalidation standards and feed into the work programme of the General Pharmaceutical Council," he said.

# Drive for quality and innovation must not be lost during financial challenges

In this session, representatives of the four UK health departments spoke about the importance of quality and innovation to deliver the savings and efficiencies that will be required within the NHS in the financially challenging times ahead. **Harriet Adcock** reports

Pharmacist practitioners will need to embrace the principles of quality, innovation, productivity and prevention, known collectively as QIPP, Keith Ridge, chief pharmaceutical officer for England, told conference participants. QIPP is currently being trumpeted by the Government as an approach that will help tackle service reform in financially challenging times.

Dr Ridge said that QIPP is a priority for the Government, being seen as the most important challenge for the NHS, alongside the current influenza pandemic.

He argued that pharmacists must not lose the momentum for change and improvement in quality created over the past few years in the current financial climate. "Over the past decade there have been record levels of investment in the NHS," he said. "This has made things much better for patients — there have been more nurses, more doctors, more pharmacists, more new technologies and so on to deal with the considerably higher levels of demand for healthcare."

These improvements, Dr Ridge explained, have been in part due to a renewed energy around improving quality. "Quality is a great prize," said Dr Ridge, "and is something we as clinicians should not allow to drift away."

He suggested there would be more to come, a greater focus on quality and on using the skills of the pharmacy team to improve health.

## Financial challenge

Dr Ridge gave a flavour of the financial challenge ahead. The economic downturn will have some direct impacts on health, for example, lower incomes leading to poorer diets, more demand for primary care, increased levels of depression and debt-related stress.

Savings will have to be found, said Dr Ridge, and for the foreseeable future, public finances will be highly stressed and will remain so, even if the wider economy recovers rapidly.

"NHS funding will enter a more challenging period in the next few years," warned Dr Ridge, but added that with the challenges, come opportunities.

"The level of real savings and efficiencies that the NHS will need to make from about 18 months time onwards are so significant and so substantial that only radical and innovative thinking, developments and change will deliver the savings and efficiencies required," he said.



Craig Strong

**Keith Ridge: only innovative thinking will deliver the savings required**

Despite the financially challenging times ahead for the NHS, it is seen as a solid foundation on which to build and develop new technologies, in partnership with the life sciences industry.

Dr Ridge argued that the life sciences industry, incorporating pharmaceutical companies and medical biotech companies, would be key to the future of the UK economy. "The intention is to ensure that the UK offers an attractive environment to life sciences companies to do business in," he said.

As part of the NHS's aim to create this environment, the National Institute for Health and Clinical Excellence will develop the innovation pass, making selective innovative medicines available on the NHS for a limited period, giving faster access to cutting edge medicines, explained Dr Ridge. Other measures include building a more integrated life sciences industry through skills development across the workforce and supporting the formation of an internationally recognised UK life sciences "super cluster" to co-ordinate work across industry, higher education and the NHS.

"I hope that you will all immediately see that this work will be very relevant to the future of healthcare and therefore to pharmacy practice in every setting," he said.

In order to build a more integrated life sciences industry there must be a continued

supply of high calibre skilled employees. To help with this a higher education forum is to be established and one of its first tasks will be to assess the curriculum of clinical pharmacology in both medicine and pharmacy.

"This is complementary to the White Paper's ongoing Modernising Pharmacy Careers programme that will, in the fullness of time, deliver pharmacy practitioners with all the necessary skills to care directly for patients and to support R&D in the UK, for example, through clinical trials."

## The drive for quality

Focusing on the QIPP programme of work, Dr Ridge explained that the aim is to drive quality while addressing the financial challenge through increased productivity. To this end, the DoH has recently appointed an NHS director for improvement and efficiency.

"There is recognition that QIPP cannot be delivered from the top down," said Dr Ridge. "Real changes have to be designed and delivered locally with the centre playing an enabling role."

He added that to do this the NHS will be encouraging the use of the four change principles that underpin Lord Darzi's Next Stage Review — co-production, subsidiarity, system alignment, and clinical ownership and leadership. On clinical ownership and

leadership, Dr Ridge argued that to deliver quality it was critical that clinicians were empowered and mobilised across the system. "Without that we will get nowhere," he said.

QIPP challenges need to be embraced at all levels, said Dr Ridge, who suggested that senior NHS managers would be looking for help and to work with many stakeholders, including pharmacy.

He pointed out that many of the initiatives in the English White Paper for pharmacy were relevant. "It goes without saying that safe, clinical and cost-effective use of medicines and pharmaceuticals will feature prominently. So local and national pharmacy leaders must try to get involved."

He argued that innovation, in its various forms, will be critical in addressing the NHS's financial challenges while still improving quality as well as in developing the future of the UK economy.

"Pharmacy practitioners, both now and more so in the future, will need to fully embrace the principles of QIPP, including having the R&D skills to support UK Plc, alongside patient care."



Craig Strong

### Norman Morrow: more emphasis on outcomes needed

Norman Morrow, chief pharmaceutical officer for Northern Ireland, argued that more emphasis needs to be placed on the measurement of outcomes. "We need to invest more time and effort in the design of initiatives and in the specification of measures that will allow for assessment of wellness and efficiency."

He also emphasised the importance of patient experience. "As we anticipate a more in-

formed society we will have to ensure a more meaningful engagement with those we treat," he said. To achieve this end, there needs to be a stronger emphasis on research and development and work at the interface between secondary and primary care, as well as a stronger focus on practice research.

Mr Morrow also argued that savings and increased productivity could be achieved by concentrating on safety and quality. "Finance often dominates but it can militate against important progress," he said.

## Role of automation and technology in improving quality

The rise of technology in pharmacy has been slow but inevitable, said Jeremy Savage, deputy chief pharmaceutical adviser to the Welsh Assembly Government.

The implementation of automated dispensing in 17 major acute hospitals across Wales has given sustained improvement in dispensing error rates of around 60 per cent and made significant improvements in the use of manpower and skill mix, he pointed out. "The sceptics said it could never be done. That is would never catch on."

The rationale for the use of automation is simple, said Mr Savage: "The robot does it more quickly, more accurately, more securely." Staff can be redeployed and their tasks focused on direct patient care.

Mr Savage conceded that some technological developments — electronic prescribing and the electronic transfer of prescriptions — have not produced the desired outcomes yet but said that progress was being made. Simple solutions such as the 2-D barcode on prescriptions were beginning to deliver the promise of reduced transcription errors, speeding up data entry and delivering ETP.

Information sharing, including the uploading of data to out-of-hours services and medical admissions wards, enables the safe transfer of patients between care settings.

To respond to well informed patients, healthcare practitioners must have access to the same resources as their patients, argued Mr Savage. "The key goal for us all must be to ensure that pharmacists in the next decade have the web at their fingertips." He said that the electronic health record would become a reality and that the public would expect and demand that pharmacists offer fast and convenient access to medicines, information and other services.

"Professionals must use the available technology to keep abreast of current hazards and alerts," he said. "We must ensure that all pharmacists are connected to these systems to ensure that adverse incident reports can be readily accessed and overcome the corporate barriers that may obstruct direct access at the moment."

The roll out of automation will continue into community pharmacy, argued Mr Savage. "Patients are demanding easier access to services — over the internet, using mail order. Why not give patients direct access to pharmacy services 24 hours a day, seven days a week?" he asked. "We have embraced automated hole in the wall technology in banking. Why not think laterally about how that can be applied to pharmacy," he suggested, adding that the "pharmacy ATM" is already a reality in Germany and Canada [see p12].

Mr Savage cited another example of a German service that involves 10 pharmacies linked together — "Medicines 24" — a service where there is always an online pharmacist available and medicines can be dispensed by robots direct to the patient. "Facilitation of remote dispensing is simply something we must do," he said.



Craig Strong

### Jeremy Savage advocates remote dispensing

### Clinician on the high street

When charged in 2005 with saving £55m from the drugs bill by 2008, it was not the financial argument but the safety and quality argument that gained involvement of the clinical community to achieve the target, Mr Morrow said.

He added that pharmacy would be critical to the quality agenda, and that clinical pharmacy services in hospitals need to be enhanced while community pharmacists need to embrace the role of clinician in the high street. "That will require a radical rethink about the design and the nature of the community contract. We have a choice here to be defensive and protective or bold and innovative," Mr Morrow concluded.

Bill Scott, chief pharmaceutical officer for Scotland, also spoke about his vision of the "clinician on the high street" and the changes needed to achieve it (*PJ*, 12 September, p261).

Responding to a question about developing the pharmacists of the future and whether five years of training was enough for a pharmacist to be in sole charge of a pharmacy, Mr Morrow said that community pharmacy could learn from the teamwork seen in hospitals.

"We have all seen young inexperienced pharmacists achieving significant things. This has occurred largely in the context of a team with good leadership." This, he argued, was missing from community pharmacy, where there is a degree of professional isolation. He suggested that once the formal five years of training had been completed, pharmacists should then move into a safe, encouraging, innovative environment. "It's about good early teamwork," he said. "And this supports the concept of group practices."

# How remote supervision is being used to benefit patients in Canada

Remotely supervised dispensing machines recently introduced in Ontario, Canada, enable pharmacy services to be extended to people living in remote areas without compromising patient safety, conference participants heard. **Gareth Malson** reports

A glimpse of how technology and remote supervision regulations can be used to extend pharmacy services to patients in remote areas was offered to participants at the British Pharmaceutical Conference. Residents of Ontario, Canada, are now able to obtain some prescription medicines, and get advice from pharmacists during the process, from dispensing machines in an increasing number of GP surgeries and emergency departments in the province.

The machines, known as “Med Centres”, have been cropping up across Ontario since provincial law was amended earlier this year. The amendments included several legislative reforms that have expanded the role of pharmacists (for example, to allow pharmacist prescribing). Legalising the remote supervision of medicines dispensing was one such amendment. Peter Suma, co-founder and chief operating officer of PharmaTrust, the company that manufactures the Med Centre, said that convincing pharmacists of the value of the machine has been no easy task.

“When I first went into the Ontario College of Pharmacy and put up a picture of our machine, their jaws hit the table,” said Mr Suma. “Anger followed; I’ve been yelled at by pharmacists, I’ve been sworn at, I’ve been



The PharmaTrust Med Centre

called the antichrist by the chief executive officer of the largest pharmacy chain in the country — he has just asked for exclusivity [for the machine].”

The technology is patient-focused and pharmacist-reliant, said Mr Suma, suggesting the machine could be a similar technological advance to that seen in the banking industry when the automatic teller was introduced. “If

you walk up to the machine and the pharmacist chooses not to answer, it’s a dead lump of metal.”

“This is about serving patients,” he went on. “It’s about extending the pharmacy to where the patient is. It is not about replacing pharmacists.”

“It’s all about the pharmacist’s professional discretion,” Mr Suma added. Therefore, if the pharmacist has any concerns about the prescription, such as the dose prescribed or the appropriateness of the medicine, he or she can instruct the patient to attend a pharmacy in person to get the prescription dispensed.

The machine offers an opportunity for pharmacists to offer a service to remote populations with poor access to a pharmacy. Mr Suma also pointed out that the machine is popular with patients, according to his company’s data. “Pharmacists are divided, patients aren’t. Like it or not, patients have come to expect a multichannel service from providers.”

He also mentioned that the machine appears to increase pharmacist-patient consultation time. “We have found that the interaction time between patients and pharmacists goes up — both patients and pharmacists have attested to that.”

Mr Suma concluded that UK pharmacists would need to decide for themselves how remote supervision should be adopted in this country. He urged participants not to dismiss remote supervision, but to consider how it can best be used to benefit patients.

## How the dispensing machine works

The PharmaTrust Med Centre works as follows:

- A patient approaches the machine and inserts his or her prescription
- The machine dials a video telephone located in the pharmacy that owns the machine — if the pharmacist answers he or she appears on a screen on the front of the machine
- If the pharmacist cannot answer, or if the patient uses the machine outside of working hours, the call is rerouted to a central office where it is taken by another pharmacist
- Both sides of the prescription are scanned and an image of it appears on screen for the pharmacist to view
- The pharmacist checks whether the machine stocks the prescribed medicine (most machines stock around 400 items but newer models stock 1,800 products)
- Speaking to the patient over a video telephone, the pharmacist obtains a full medication history and confirms whether the patient is allergic to any medicines (this information is used to create a patient profile, which is updated every time a supply is made)
- If the pharmacist is happy for the medicine to be supplied, the machine is instructed to select, dispense and label the product
- Before the product is released, the pharmacist is shown a full breakdown of its manufacturing information (for example, batch number, expiry date, product weight) and can view the dispensed medicine from several angles using cameras mounted inside the machine
- Once the pharmacist is happy that the medicine has been dispensed correctly, he or she can instruct the dispensing door on the machine to open and the patient can take the medicine
- The pharmacist provides any required counselling over the telephone and the patient is given a chance to ask any questions before the process is completed

# Simulated patient project to benefit all

Benedict Lam reports on the Royal Pharmaceutical Society's simulated patient project and on the importance of pharmacists in reclassifying drugs

A simulated patient is an individual who is trained to visit a pharmacy to enact a standardised scenario, said Margaret Watson, senior research fellow, University of Aberdeen. A common descriptor for a simulated patient is "mystery shopper", she added.

Dr Watson explained that the purpose of the simulated patient project, which is being developed by the Royal Pharmaceutical Society and the National Pharmacy Association, is:

- To measure current practice in community pharmacy
- To assess the effects of intervention
- To change behaviour (of pharmacists and pharmacy staff)

She believes that there are many benefits to using the simulated patient project, including that it is a rigorous and robust method of measurement, it is internationally applicable, it assesses actual behaviour (of pharmacists or pharmacy staff), it resembles "real" patients and it avoids the Hawthorne effect [whereby individuals improve an aspect of their behaviour being experimentally measured simply in response to the fact that they are being studied].

The project involves a simulated patient making a visit to a pharmacy. After the scenario, the simulated patient will leave the pharmacy, prepare feedback and return to the pharmacy (on the same day). He or she will identify himself or herself and provide feedback to the member of staff involved (preferably in the presence of a pharmacist). The simulated patient will ask the member of staff how he or she felt the consultation went and what aspects of the consultation could he or she improve on. This, Dr Watson explained,



**Margaret Watson: feedback needed to reinforce good practice**

encourages those involved to identify how they could improve on their behaviour in the future. A feedback form is provided to the pharmacy and detailed feedback will be sent to the pharmacy a few weeks after the visit.

Dr Watson stressed that feedback is needed because it promotes and reinforces good practice and corrects poor performance. She added that community pharmacists are often isolated health professionals and, by giving feedback about their service, they can be informed of what is going well and what is not going so well.

Valerie De Ruyter, project manager for the simulated patient project, Royal

Pharmaceutical Society, said that the project only involves pharmacy medicines and is a measure of good practice (not fitness-to-practise). Phase 1 of the project will involve 5 per cent of all community pharmacies in Britain.

The six simulated patient scenarios are:

- Potential drug interactions
- POM-to-P products
- Medicines that have abuse potential
- Medicines that have misuse potential
- Patient is not present in the pharmacy (ie, the simulated patient is buying a medicine for someone else)
- Confidentiality issues

Ms De Ruyter believes that there are many benefits for pharmacists, patients and pharmaceutical companies. Pharmacists, she said, could improve their performance, improve the reputation of the profession, and use the experience as a contribution to their continuing professional development and as an evidence base of their good practice.

For patients, the programme could lead to them gaining confidence in community pharmacists as primary care providers and being educated towards self-care.

The benefits for pharmaceutical companies could include having access to aggregated data that stem from the project, being viewed as supporters of good clinical practice, an increase in the market for pharmacy medicines and an increase in the potential for medicines reclassification, she said.

Ms De Ruyter explained that phase I of the project will last for approximately 11 months and the start date would depend on funding (financial contributions are being sought from pharmaceutical companies).

## UK is European leader in reclassification of drugs

Pharmacists are key players in the reclassification process, said Colette McCreedy, specialist in self-medication at the Medicines and Healthcare products Regulatory Agency.

She said that, since the publication of the NHS plan in 2000, many NHS policy documents have made reference to making more medicines available without prescription and empowering people to look after themselves. Also, the pharmacy White Paper in England and pharmacy policy documents in the other UK countries envisage a greater role for pharmacists in self-care, public health and screening, and all of these can be supported by POM-to-P reclassification.

Mrs McCreedy emphasised that the ability of pharmacists to deliver the rigorous type of supervision and professional intervention re-

quired to supply medicines safely and effectively without prescription — whether the supply is made by a pharmacist or by members of the pharmacy team — is a key factor in deciding whether a medicine is suitable for reclassification. This, she said, has contributed to the increasing range of medicines that we see in pharmacies today.

Mrs McCreedy believes that the UK is the European (if not world) leader in reclassification of medicines, citing the recent reclassification of azithromycin for the treatment of chlamydia as an example. Medicines that have been reclassified at EU level, such as orlistat, are also emerging. These medicines become available at the same time in all 27 member states.

Mrs McCreedy believes that the UK has an advantage with regards to reclassification

because UK legislation allows the MHRA to put in place safeguards that ensure safe sales and supplies involving pharmacists. Many member states do not have the legislative framework to do this, she added.

However, Mrs McCreedy said that with this ground-breaking work comes the need to continuously monitor safety in use, such as using the yellow card reporting system.

Moreover, pharmacists can help by supporting risk minimisation measures that the MHRA puts in place when safety in use or misuse is discovered, Mrs McCreedy said. For example, pharmacy controls have ensured those who seek to buy pseudoephedrine from pharmacies for the illicit manufacture of crystal methamphetamine have not succeeded.

# Pharmacist prescribers: latest lessons and developments from the field

Beth Taylor, Anne Adams and Zoe Girdis report on a workshop examining the latest developments and research relating to prescribing by pharmacists

Current issues for pharmacist prescribers were explored in this interactive workshop session, which was introduced by Beth Taylor, member of the English Pharmacy Board.

Throughout the session, ideas on how the new professional leadership body could support pharmacist independent prescribers (PIPs) at both national and local levels were captured to inform future developments.

Alison Blenkinsopp, professor of the practice of pharmacy at Keele University, presented some emerging findings from the national evaluation of nurse and pharmacist independent prescribing, of which she is the pharmacy lead. Her presentation focused on clinical governance and risk management strategies, based on survey results for PIPs and nurse independent prescribers (NIPs), and a telephone survey of trust non-medical prescribing leads.

Over 80 per cent of the 142 PIPs who responded practised in general practice or NHS trust settings and the most common clinical conditions treated were (in decreasing order) hypertension, coronary heart disease, cardiology, diabetes, care of older people, asthma and chronic obstructive pulmonary disease. About half of trusts have a written plan or strategy to guide non-medical prescribers' (NMPs) development, and most NIPs and PIPs report having a regular appraisal and personal development plan, although these were reported by higher percentages of NMPs in hospitals than in primary care.

A range of tools is being used to quality assure NMP prescribing, including prescribing activity reports, significant event analysis, peer review and evidence portfolios. There is also scope to increase the use of patient feedback to inform the future development of PIP services, and Professor Blenkinsopp emphasised that commissioners have moved on from simple patient satisfaction surveys to a greater focus on patient experience and comparisons with other options.

Karen O'Brien, associate director of primary care commissioning for NHS Manchester, has a pharmacy background and gave a commissioner's viewpoint. She emphasised that pharmacists must understand the NHS commissioning cycle and its implications when developing proposals using PIPs. Commissioners have choices on routes for obtaining medicines and will want to make value for money comparisons, she said. World class commissioning competencies may help to shift attention to prevention and well-being, where pharmacy strengths may lie, she added.



Craig Strong

## Alison Blenkinsopp presented findings from the national prescribing evaluation

As a commissioner, Mrs O'Brien looks for opportunities where pharmacists can best serve the local population's needs. These may

include: GP practices that underperform under the quality and outcomes framework or do not want enhanced services such as sexual health; prescribing statins as part of the NHS health check; and clinics for long-term conditions and hypertension.

Mrs O'Brien encouraged pharmacists to be proactive, to engage with the primary care trust strategy at an early stage and, as a "willing provider", to be on the lookout for advertisements for tenders and other opportunities. National bodies could help to support pharmacists in the tendering and bidding processes, she suggested.

Participants at the workshop (who included many active PIPs) believed that most successful prescribers had already established a long-term trusting relationship with their GP or doctor colleagues. There was support for "pharmacist prescriber champion" roles, so they could more effectively pitch to commissioners.

## Current issues

During group discussions, participants considered the following current issues:

### What might be the niche market for PIP services?

- Needs are emerging within specialist teams, such as addiction services, care homes support, clozapine clinics, skin allergy testing
- In clinical areas, such as anticoagulation, hypertension
- In areas involving pharmaceutical expertise, such as therapeutics/kinetics, formulation, interactions, which add value beyond nurse prescribers
- Improving patient experience and enhancing the overall service, such as sexual health, public health campaigns, healthy living centres

### What support systems would need to be in place?

- Access to medical and administrative support are fundamental
- Robust referral pathway and clinical governance
- Funding via specialist clinical teams, especially regarding meeting targets
- Multiprofessional training — this supports PIPs because it promotes understanding of their contribution
- More case studies which show how PIPs and also doctors and nurses work effectively together within a service (not as sole practitioners)

### What value is a pharmacist prescriber adding to this service?

- Stopping ineffective or unnecessary prescribing
- Complementing the skills of other non-medical prescribers, for example, nurse and pharmacist prescribers
- Improving hard outcomes, such as GP callouts, hospital admission, falls and fractures, benzodiazepine prescribing and better end-of-life care

### What seem to be the factors that have determined success?

- A critical mass of qualified pharmacist prescribers available locally — if they are spread too thinly this deters commissioners from using them
- Creating an evidence base through pre- and post-service audits
- Starting small
- Staying within competencies

The overall ambition is to provide a convenient, comprehensive service within a PIP's competence.

# Communication and integration key to successful medicines use reviews

Participants heard how pharmacists are delivering medicines use reviews in practice and how the Royal Pharmaceutical Society's audit tool can help to demonstrate the quality and benefit of MURs at a national level. **Heidi Wright** reports

Communication is the key to medicines use reviews (MURs), said Samiah Tamba, a community pharmacist, who spoke of her experience of setting up a successful MUR service in the Midlands. This meant not just communication with the patient who is undergoing the MUR, but communication with other healthcare professionals, for example, the patient's GP and district nurses, she added.

Miss Tamba has worked in her pharmacy for over 15 years so has had the opportunity to build up good relationships with local GP practices and this has helped with the implementation of the MUR service.

Shane Gordon, a GP based in Colchester, Essex, talked about the need to integrate MURs into primary care trust plans and to make sure that they are targeted at patients who will get the most benefit from them.

Dr Gordon described the service in Colchester, where MURs are undertaken after discharge from hospital. He emphasised the importance of working with other healthcare professionals for the benefit of patients.

Kevin Noble, a PCT pharmacist based in the Isle of Wight, spoke of his involvement in setting up targeted MURs — MURs which have been targeted towards specific patient groups, in this case people with asthma. This approach has proved highly successful and the



Session attendees took part in a debate about MURs

service is being evaluated (*PJ*, 31 January 2009, p99). Targeting MURs makes them relevant to the PCT and to local practices, he said.

The final speaker was Heidi Wright, head of practice at the Royal Pharmaceutical Society. She described a new MUR audit tool that has been developed by the Society in collaboration with the Royal College of General Practitioners and the Clinical Audit Support Centre. She talked about the various ways of implementing this audit and how data

would be collected nationally to help demonstrate the quality and benefit of MURs at a national level. The tool was launched in July.

Session attendees then took part in a lively debate about MURs, concluding that, although they were perhaps not introduced in the best way, MURs have now proved to be beneficial providing they are used in the right way — communicated properly, targeted and integrated, and focused on quality rather than quantity.

## Student wins prize for new prison pharmacist logo

A logo is essential to recognising a particular organisation or specialty. To that end, pharmacists who work in secure establishments recently embarked on finding a suitable logo to identify their group.

A competition was launched at the annual British Pharmaceutical Students' Association conference, inviting students to design a logo for the secure environment pharmacists group. The prize was a visit to a prison and £75 of vouchers donated by RPS Publishing.

The photograph shows the award winner Jainaba Nije from Portsmouth University (centre) receiving her prize from (left to right) Davan Eustace, representing the Secure Environment Pharmacists Group, Bob Bolick, managing director RPS Publishing, and Jonathan Mason, national clinical director for primary care and community pharmacy in England. The award was presented at the BPSA stand during BPC 2009.



# Health checks: benefits and challenges

**Benedict Lam, Nicola Cree and Francesca Rivers** report on progress with NHS Health Checks and on the research poster winners at this year's BPC

One of the aims of NHS Health Checks [a vascular risk management programme offered to people in England aged 40 to 74 years] (*PJ*, 11 April, p417) is to offer straightforward risk assessment for diseases affecting the cardiovascular system, including diabetes and chronic kidney disease, said Richard Daniszewski, vice-chairman of the English Pharmacy Board.

The longer-term aims, he added, are to reduce premature death from related vascular conditions, including coronary heart disease, chronic kidney disease, diabetes, stroke, transient ischaemic attacks and peripheral arterial disease. Also, it aims to identify those in the population at risk of vascular disease earlier rather than later and narrow inequalities in the number of premature deaths.

Mr Daniszewski said it is estimated, based on known effective management applied to individuals who are at high risk, that the pro-

gramme will prevent 1,600 heart attacks and strokes, 650 cardiovascular deaths and 4,000 people from developing diabetes per year.

## Programme roll out

The scheme, he said, was introduced on 1 April 2009 across all primary care trusts in England and they will be expected to implement and deliver the service between now and 2010. The economic modelling underpinning the vascular checks programme is based on the assumption that PCTs will complete roll out by 2012–13. However, Mr Daniszewski emphasised, the actual pace of implementation is for PCTs to decide — some will be faster than others.

Spearhead PCTs [the 88 most health-deprived areas in England] are likely to be the first to receive funding to help implement the programme, Mr Daniszewski suggested. Vascular disease also makes up approximately



**Richard Daniszewski: spearhead PCTs likely to receive funding first**

one-third of the difference in life expectancy between spearhead areas and the rest of England.

## Opportunities and challenges for pharmacists offering NHS Health Checks

Pharmacists offering NHS Health Checks can include people who are not ill but may need to modify their lifestyle, while GPs are trained to deal with those who are ill, suggested Helen Williams, consultant pharmacist, Southwark Health and Social Care.

Because most pharmacies are open for long hours, including evenings and weekends, they are ideal places from which to offer health checks and identify those who may be at risk of vascular disease, Miss Williams argued. They are also suited to offering lifestyle advice as well as other services, for example, smoking cessation, signposting to other services, like local exercise programmes, or to making referrals to GPs.

However, Miss Williams believes there are issues that need to be considered with pharmacies offering health checks. These include patient engagement,

delivering lifestyle interventions and making appropriate medical interventions. Also, to reduce inequality, consideration needs to be given to certain populations, for example, those who are not registered with a GP and ethnic minority groups.

Another barrier to offering health checks is that, not only does a pharmacy need to have a consultation room, it also needs to be equipped with a wash basin. Many pharmacies with consultation rooms do not have this facility, said Miss Williams. Continuity of service also needs to be considered, for example, locums who are not accredited to provide the health checks working in pharmacies that usually offer the service.

Moreover, pharmacy needs to maintain a competitive edge with offering health checks since other healthcare professionals, such as optometrists and dentists, want to provide this service as well, Miss Williams emphasised.

## Practice poster prizes Awards given for science posters

An assessment of treatment culture on the prescribing of psychoactive medication in nursing homes for older people won first prize at the practice poster session during the British Pharmaceutical Conference.

Ailis Donnelly, of Queen's University, Belfast, was presented with an Amazon.com voucher for £150 by Peter Noyce, BPC Practice Chairman, at a reception sponsored by Boots The Chemists. The prizes were sponsored by the Royal Pharmaceutical Society.

Second and third prizes, vouchers for £100 and £50, respectively, were awarded to Peter Knapp, of the University of Leeds, for a poster entitled "User testing of participant information for a phase 3 trial of cholesterol-lowering therapy", and to Anne Hinchliffe, of Cardiff University, for a poster entitled "The impact of community pharmacy advice on safe storage and administration of medicines in adult care homes".

A study of a polyamidoamine dendrimer-based drug delivery system to bypass the P-glycoprotein efflux transporter was awarded one of three prizes for best science poster of the day on the penultimate day of this year's British Pharmaceutical Conference. H. M. Teow, of the University of Central Lancashire, was presented with a cheque for £100 by Dave Elder, a director at GlaxoSmithKline, which sponsored the awards along with the Academy of Pharmaceutical Sciences.

Also awarded £100 prizes for best science poster of the day were John Willets, from the University of Birmingham, for a poster entitled "Investigation into the effects of blend energy input at different scales on alpha-lactose monohydrate", and Oladayo Adenuga, from the University of Brighton, for a poster entitled "Development of an *in vitro* model for oral biofilm studies". The teams behind both of

these posters included researchers from GSK.

On the final day of the conference, Huda Zughaid, of King's College London, won a £150 prize for her poster on solubilisation of steroid drugs by simulated intestinal fluids containing lipids.

Ben Staley, of the University of Manchester, and Melinda Chau, from the University of Wolverhampton, also won £150 prizes for their posters.

Mr Staley's poster was entitled "Observation of the uptake of TAT peptide at nanomolar concentration" and Miss Chau's poster was entitled "Quantitative analysis of konjac glucomannan (KGM) extracted from corms of *Amorphophallus konjac*".

The prizes were presented to all three winners by Eddie French, chairman of the Academy of Pharmaceutical Sciences, and James Butler, scientific investigator, GSK.

# Speed dating sessions with specialist and advanced level practitioners

This session, organised by the Royal Pharmaceutical Society's Community Pharmacists Group, featured pharmacists from community and secondary care who led a speed dating style meeting to describe their experiences of advanced and specialist practice. **Nina Barnett** reports

There is no agreed definition for advanced and specialist practice and a lack of national pharmacy accreditation for individuals across all areas of practice, said Nina Barnett, chairman of the consultant pharmacists group for England, as she outlined the issues around defining advanced and specialist practice.

Ms Barnett described the consultant pharmacist post, and practitioners within those posts, as well as the role of pharmacists with a special interest. Both of these roles are defined by Department of Health guidance and underpinned by the advanced and consultant level competency framework, she explained.

Ms Barnett outlined the potential characteristics of a higher level practitioner, including:

- Expertise in an area of practice
- Multidisciplinary working
- Use of judgement and reasoning to support clinical decisions where clear evidence is not apparent

The place of pharmacist prescribing in terms of higher level practice, now and in the future, was considered. Ms Barnett suggested that some prescribing by pharmacists may be undertaken soon after qualification in the future whereas other areas of prescribing might remain a higher level practice activity.

Carol Evans, head of professional development at the Royal Pharmaceutical Society, de-

scribed the key objectives of the Society's advanced and specialist practice project. These included combining competency frameworks to provide support for national recognition of advanced and specialist practice, and personal achievement awards for individual pharmacists.

Mrs Evans explained the goals of the project group, which followed from the Transitional Committee report on improved, advanced and specialist practice, and updated participants with current progress, outlining the project timetable.

Stakeholder reference meetings started in July 2009 and were due to continue through 2010. There is a working group, which includes representation from all sectors of the profession in England, Scotland and Wales, and a wider reference group to

ensure maximal stakeholder involvement, she explained.

## Speed dating

The remainder of the session was devoted to group discussions. These were based on the "speed dating" concept but allowed 20 minutes per table for each "expert" to be interviewed by conference participants. The experts were two prescribers, two consultant pharmacists and two pharmacists with a special interest (see Panel).

The idea of the session was to give participants an opportunity to find out how these pathfinder postholders reached their current positions, what their roles entailed and the opportunities and challenges that they had experienced along the way.

## The experts

The pharmacist prescribers included Zoe Girdis, primary care prescriber at Portsmouth Primary Care Trust, who specialises in cardiovascular disease and obesity, and Nina Barnett, prescriber in intermediate care for older people, Harrow PCT, who is also a consultant pharmacist.

The consultant pharmacists were Steve Williams, who specialises in medicine and patient safety and is based at the University Hospital of South Manchester, with a one day per week at Manchester University, and Helen Meynell, from Doncaster and Bassetlaw hospital, who provides a referral service for pharmacists caring for patients with complex pharmaceutical care needs, particularly in the areas of respiratory medicine and palliative care. These are two different models of consultant practice, both of which fall within the DoH guidance for the post.

The two pharmacists with a special interest were Linda Hirst, from Bradford and Airedale PCT, and Janine Barnes, from Dudley PCT. Ms Hirst provides an anticoagulation monitoring services at a weekly clinic and Ms Barnes provides a specialist service in neurology at Dudley PCT.

## Young pharmacists learn what careers are possible



PJ editor Olivia Timbs (centre) chairs the annual BPC-PJ Careers Forum

Craig Strong

# Analysis of problems in primary care

Gareth Malson and Nicola Cree report on problems in primary care and how pharmacists can reduce adverse drug reactions

The reason for varying levels of clinical services commissioned from pharmacies across the UK is not due to a lack of national policy, said David Jenner, practice-based commissioning lead for the NHS Alliance. "The current Government has not been idle in producing policy and documents," he said, citing documents such as "World class commissioning" and Lord Darzi's next stage review of the NHS as examples. These policies promote commissioning from all primary care clinicians, not just GPs. However, he went on to say: "The truth is: it is all about GPs because we hold registered lists [of patients] and we, directly or indirectly, commit most of the resources by prescribing or referring."

The problems are financial, says Dr Jenner, and the use of Payment by Results (PbR) to pay hospitals for the care they provide has not helped the commissioning of services from primary care providers. He said PbR was, in fact, "payment by activity" and that it had done little to improve healthcare quality. "It has driven capacity, it has driven supply, it has helped us meet targets, but it has cost a lot of money," he said. "As a commissioner, I cannot set a budget with my [acute] trust because if they do more work, they get paid more." He went on: "There are no disincentives for acute trusts to manage demand."

## Lack of commissioning

Most pharmacists will not have noticed a difference since practice-based commissioning began, said Dr Jenner. Although he accepted



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## David Jenner: Payment by Results has not helped commissioning

that some commissioning consortia were opting to keep money in general practice, he does not believe that is the crux of the problem. "A lot of my colleagues would commission more from pharmacy if they could, but the access to the care record is one of the biggest stumbling blocks for pharmacy to compete with general practice," he explained.

He expressed concern that some pharmacists working for multiples had told him that

staffing levels were being reduced because of the credit crunch. This meant that there were not enough staff to deliver enhanced services.

## Future working

Dr Jenner understands that most primary care commissioners have been told to look for 20 per cent "efficiency cuts" over the next five years. "We know there are tough decisions ahead but, at the moment, we don't know what that will mean."

Nonetheless, he believes this will only be achieved through collaboration between all healthcare providers. In particular, he highlighted collaboration between pharmacy and general practice: "Couldn't we be working closer together? Couldn't pharmacies move into GP practices more?"

"Pharmacists sometimes feel restricted from doing clinical services by the need to supervise dispensing but why can't pharmacists provide clinical services through general practices? Why can't people have joint contracts?" He admitted there were legislative issues to resolve, and issues regarding conflict of interests, but concluded: "It just makes such good sense."

Although he acknowledged that Tory policy was still evolving, he hypothesised that a Conservative government would promote competition among healthcare providers. This could lead to control of entry for pharmacies being deregulated, a devaluation of PbR payments and a cap on acute trust incomes, plus a renegotiation of the community pharmacy and the GP contract.

# Reducing preventable adverse drug reactions

Researchers in the US estimate that, in long-term care settings, for every dollar spent on drug and nursing facilities \$1.33 is spent on treating drug-related problems, said Neil Mackinnon, associate professor, Dalhousie University, Canada.

Research from the Commonwealth Fund has shown that 13 per cent of patients in the UK have reported having experienced a medication, medical or laboratory error in the past two years, Dr Mackinnon said. This compares with 17 per cent in Canada and 20 per cent in Australia and the US.

Quoting a physician at Harvard, Massachusetts, Dr Mackinnon told the conference that any symptom in an elderly patient should be considered a drug side effect until proved otherwise.

There are eight key factors (see Panel) that constitute a complete and safe medication use system. If one of these key things is missing, patients are at increased risk of experiencing an adverse event, he said.

There are a number of things that pharmacists can do to reduce adverse drug events. Pharmacists should ensure that for every prescription they dispense, they know why the patient is taking the medicine, not just what the medicine is for. Pharmacists should also try to eliminate the "quality tax" — where one pharmacy provides better care than another when they receive the same reimbursement, Dr Mackinnon said.

Pharmacists should be engaging patients in medicines use management and providing family level pharmaceutical care, that is, care that you would like your family to receive. Pharmacists should also be aiming for customer satisfaction and should ensure that they implement best-demonstrated practices, he said.

Pharmacists should be considering what they can do that will change a patient's quality of life, Dr Mackinnon added.

In order to help raise their profile, pharmacists should wear a badge that says "Ask

me about your medicines". Pharmacists can also improve their relationships with prescribers, Dr Mackinnon suggested, by providing positive feedback since the majority of interactions prescribers have with pharmacists are because of problems with prescriptions.

## Medication use system

Eight key factors constitute a complete and safe medication use system:

- Timely problem recognition and diagnosis
- Safe, accessible, cost-effective medicines
- Appropriate prescribing
- Distribution and tailored patient advice
- Patient participation and intelligent adherence
- Monitoring
- Documentation and communication
- System evaluation, measurement and improvement

# Innovation central to taking services forward in challenging financial times

Hospital tsar Martin Stephens highlighted how pharmacists can help the NHS to maximise productivity within limited resources. **Harriet Adcock** reports

Innovation will be central to taking pharmacy services forward in challenging financial times, argued Martin Stephens, national clinical director for hospital pharmacy in England, in his address to conference participants.

He explained that, in the past, the NHS had often responded to funding squeezes by closing a ward or shutting down a service. "That is not a choice for the NHS anymore," he said, pointing out that such moves led to decreases in efficiency, patients becoming more ill and quality of care dropping.

"We need innovation to drive up productivity and improve quality. Or at least to sustain it," he said.

Mr Stephens highlighted the need for quality, innovation, productivity and prevention, principles also emphasised by Keith Ridge, chief pharmaceutical officer for England, in his speech to the conference (see p10).

These principles, known collectively as QIPP, are a priority for the Department of Health and feed into its work to see the NHS through the funding crisis.

"Good use of medicines is part of this," argued Mr Stephens, who has been asked by the DoH to lead a QIPP project in secondary and tertiary care. "Avoiding admissions related to poor medicines use, whether errors or adverse events, or failing to optimise care, these are important areas where we can increase quality and make the service more efficient."

In his role at the top table, Mr Stephens said he would point out the importance, not just of cost-effective medicines, but of using medicines to make the whole of healthcare cost-effective.

Transfer of patients between care settings is an area of tension that can be improved to deliver quality and productivity, suggested Mr

Stephens, who highlighted a forthcoming report from the Care Quality Commission on this topic. The report, which would emphasise the need for timely, clear and accurate information about medicines when patients are discharged from hospital, would be an opportunity for pharmacists to raise the issue within their own organisations.

Mr Stephens signalled the prospect of post-discharge medicines use reviews as a national directed service. "These must be used wisely and be aimed at patients most likely to benefit," argued Mr Stephens. The issue is currently being discussed by the Pharmaceutical Services Negotiating Committee and NHS Employers as part of their negotiations on the community pharmacy contract for England, he said.

"It would be great if secondary care could refer particular patients to community pharmacy as a way of using this service. This is certainly an area for local discussion between hospitals and community pharmacy through local pharmaceutical committees once it has been established."

Another area in need of innovation is the way the health service makes use of pharmacists as prescribers in secondary care. Pharmacists are leading the way in prescribing on admission, he said, through taking the harder to manage therapies, such as surgical prophylaxis and post-operative antibiotics. "All this could lead to safer, better care and more efficient use of resources."

Mr Stephens also argued that, going forward, patient experience of the health service would be just as important as the outcomes delivered. "As front-line practitioners and service managers it does us good to look at our services from a patient's perspective. Are we engaging with patients enough, do we treat them with dignity, are we serious enough about patient confidentiality, and do



Craig Strong

**Martin Stephens: engage with patients**

we keep people waiting too long outside our dispensaries," he asked.

Clinical audits often look broadly at whether a series of standards are being met. "This is important . . . but high-quality care is also about meeting individual needs."

There is a lot more that pharmacists can do in terms of patient experience and individualising medicines regimens, Mr Stephens argued.

Returning to the financial challenges faced by the NHS, Mr Stephens said that pharmacists' ability to innovate would be needed to help the NHS maximise its productivity with limited financial resources.

And although financial recovery in the economy might come sooner, "gaps in public funding will be with us for much longer", a situation he described as the most challenging period pharmacists are likely to see in their careers. "We have got 18 months to get ready for harder times," he warned.

Pharmacy leaders at all levels need to respond to this challenge, he told conference participants, calling on chief pharmacists to be open to automation and new ways of working. "Front-line teams need to be fully engaged," Mr Stephens added. "We really need your creativity and your ability to innovate. That will be the solution."

Mr Stephens's counterpart for primary care and community pharmacy, Jonathan Mason, also spoke about transfer of patients between primary and secondary care and the need to develop a set of quality indicators for pharmacy (*PJ*, 12 September 2009, p260 and p261).



Craig Strong

**Conference participants listen to Mr Stephen's address**

# Pharmacy practice research reviewed

One hundred and two practice research papers were presented at the 2009 British Pharmaceutical Conference. **Pamela Mason** reviews a selection of the most interesting papers, including studies on medicines use reviews, non-prescription medicines, public health and workforce issues

Change is the watchword this year. Reading through all the practice research papers presented at the BPC 2009, I was conscious of a profession passing through huge change. Indeed, change in relation to practice is mentioned more than 50 times in the papers overall.

Pharmacy services — from medicines use reviews (MURs) to public health — are also, not surprisingly, a strong theme. My overall impression is that, despite significant workload issues, which are also the focus of several papers, pharmacy is vibrant with the profession at all levels working towards a sustainable future.

Our journey through this year's papers starts with MURs, then moves on to practice around non-prescription medicines. Next comes public health, patient safety, then learning and development before ending with workforce issues in the pharmacy team.

## Medicines use reviews

Much of the research on MURs was about opinions: the opinions of patients, pharmacists and doctors.

**Youssef** (Derby and DeMontfort University, Leicester) found that patients on warfarin benefit from a structured MUR. In this study, patients having warfarin MURs were recruited in a community pharmacy in Derby to fill in a patient satisfaction survey regarding their experience of MUR. Of the 17 survey respondents, 15 felt they had learnt what to do if they missed a warfarin dose and 14 had learnt when to take their warfarin. Patients also felt they had learnt about food supplement interactions and the importance of avoiding alcohol binge drinking. Patients' attitudes towards pharmacists discussing warfarin treatment with them were extremely positive and most felt they would be happy to have their international normalised ratio (INR) measured in the pharmacy.

In another study looking at patients' perceptions of MURs, in this case in a rural community, **Patel and Lefteri** (School of Pharmacy, University of Hertfordshire), also found that patients value MURs. This was a study involving a face-to-face questionnaire on 83 patients, 29 of whom had received an MUR carried out in the study pharmacy. Among these patients, 90 per cent claimed the MUR had improved their knowledge of their medicines. Eighty three per cent rated the service as good and a further 17 per cent rated it as excellent. All patients said they would recommend an MUR to others.

So, if patients have positive views of MURs, what are pharmacists' perceptions? **Khideja** (Aston University, Birmingham) surveyed community pharmacists via a focus



Medicines use reviews valued by patients

group and 21 semi-structured telephone interviews. Community pharmacists' understanding of the term MUR and their role in providing MURs varied widely from thinking they involved clinical interventions to giving basic information on use of medicines. Opinions also varied as to the purpose of MUR accreditation and the extent to which the training prepared the pharmacist to undertake MURs. But all agreed that ongoing training is vital.

In a further study from the same department **Bassi and Wood** (Aston University) surveyed 100 community pharmacists and found that employee pharmacists still think that quality of MURs is being compromised in the effort to achieve target numbers. Interestingly, more than half the pharmacists thought that patients were not aware of the MUR service and that changing the name of the service from MUR to, for example, "medicines check-up" might improve awareness.

Moving on to GPs' views of MURs, a study by **Patel** (King's College, London) and **Rosenbloom** found that a majority of GPs believed that MURs did not resolve patients' problems or only partially did so. This study surveyed 135 local GP practices, from which 61 GPs replied. When asked what they wanted MURs to achieve, GPs said it was vital that MURs gave patients understanding of how to take their medicines. Most GPs also wanted MURs to be able to identify and resolve poor or ineffective use of medicines, es-

tablish patients' anticoagulant clinic attendance and frequency of INR monitoring, identify drug interactions and side effects that may affect compliance, establish actual medicines use and reduce medicines wastage.

MURs provide a useful opportunity for community pharmacists to review non-prescribed products. However, a study by **John** (Welsh School of Pharmacy, Cardiff University) *et al* found that few MURs appeared to include the use of non-prescribed products. The researchers evaluated all MUR forms over a three-year period in six pharmacies from one multiple in one city. Of the 1,639 MUR forms completed, only 22 contained a reference to a non-prescribed product, which was actioned, for example by referral to the GP. The products concerned were a laxative, an antacid, a sedating antihistamine, a topical antifungal, aspirin, paracetamol and food supplements.

## Non-prescription medicines

Continuing with the theme of non-prescription medicines, a study by **Hanna and Hughes** (Queen's University, Belfast) evaluated pharmacists' attitudes in relation to the application of an often poor evidence base for over-the-counter (OTC) medicines. A questionnaire was sent to all 529 registered community pharmacists in Northern Ireland, of whom 209 (39 per cent) responded. Most respondents were familiar with the concept of evidence-based practice, but when thinking about the effectiveness of OTC medi-

Chris Rose

cines, they tended to rely on feedback from patients, healthcare colleagues and personal or family use of OTC medicines rather than the evidence base.

Prescription-only to pharmacy medicine switches are welcomed by pharmacists according to research conducted by **Colquhoun** (Health Attitudes Direct, Tunbridge Wells) *et al*. The majority of the 40 community pharmacists participating in this survey said POM-to-P switch products add value to the profession, allowing the provision of quality products and empowering pharmacists. The main things that encouraged recommendation of a switched product were belief in the therapeutic superiority of the product, exclusive pharmacy availability and opportunity for patient counselling. Major barriers to recommending switched products included the cost to the patient, lack of counselling time and the need to fill in a questionnaire to see if the product was suitable for the patient.

Turning to specific POM-to-P switches, **Chappell** (University of Bath) *et al* explored the views of community pharmacists and potential patients on the reclassification of azithromycin for the treatment of chlamydia infection. Among the 230 pharmacist who responded to the questionnaire, 78 per cent believed that reclassification would increase public awareness of chlamydia and 87 per cent believed it was positive for community pharmacists. A majority also said that convenience and rapid access would encourage patients to use pharmacies. Most of the 981 potential patients surveyed said they would use a pharmacy as a source of information, testing and product supply for future chlamydia treatment. Cost was an issue, with 81 per cent of those surveyed being willing to pay up to £20 for treatment. Pharmacists considered the costs of over-the-counter testing and treatment prohibitive for those under the age of 25 years.

Concerns about inappropriate use of chloramphenicol eye preparations following reclassification were tackled by **Walker** (National Public Health Service, Cardiff) and **Hinchliffe**. This study involved a retrospective analysis of prescribing data from 2003–08 and OTC sale data from 2005–08. The aim was to see if reclassification of chloramphenicol eye drops and eye ointment had any impact on prescription volume and overall use of ophthalmic chloramphenicol. What happened was that the number of prescription items for ophthalmic chloramphenicol did not change following introduction of OTC chloramphenicol. However, sales of chloramphenicol exceeded 27 per cent of the prescription volume, indicating increased use of chloramphenicol overall.

## Public health

Reduction and prevention of alcohol misuse is a key public health aim, and **Dhital** (King's College, London) *et al* investigated whether people would use community pharmacies for an alcohol screening service. Interestingly, in

this study, there seemed to be almost twice the proportion of risky drinkers among pharmacy customers compared with estimates of the proportion within the general population. Regardless of their drinking status, however, most customers were interested in using a pharmacy-based alcohol service.

If pharmacists have not been heavily involved in alcohol services, they are increasingly providing public health services around cardiovascular disease. **Horgan** (NHS South Birmingham, Birmingham) *et al* surveyed clients participating in the "Heart MOT", a community pharmacy vascular risk assessment service delivered in areas of deprivation. Of the 176 clients who responded to the questionnaire (44 per cent), 98 per cent said they were happy with the service and all but two said they would recommend it to others. Thirty eight clients identified areas for improvement, including space and privacy of the pharmacy consulting room and the need for more advertising.

Time is an important factor in providing any pharmacy service. **Thornley** (Boots UK, Nottingham) *et al* looked at consultation times with clients using the Boots "Healthy heart" service. Among the 214 clients for whom consultation times were recorded, 78 per cent chose the tier 3 service, which included measurement of blood pressure, body mass index, waist circumference, blood glucose, total cholesterol, and high density lipoprotein (HDL) cholesterol, to enable calculation of lipid fractions. Clients were referred to their GP, signposted to other services or given lifestyle advice as appropriate. About half of these tier 3 consultations, including paperwork, lasted between 21 and 30 minutes and 94 per cent were conducted within 30 minutes.

Medicines-related falls can be a cause of considerable morbidity in older people, and **Hall** (Leicester, School of Pharmacy, De Montfort University) *et al* have developed a screening tool designed to assess the risk of falls associated with medicines. The tool was piloted in 101 patients over the age of 65 years. It was able to differentiate between patients at low, medium and high risk of falls, in that there was a significant difference between the risk seen in patients taking more than 10 medicines compared with those taking fewer than four.

## Patient safety

Adverse drug reactions (ADRs) are a reporting category in the National Patient Safety Agency hospital patient safety incident reporting system. **Davies** (Royal Liverpool and Broadgreen University Hospitals NHS Trust) *et al*, set out to compare this system with the Medicine and Healthcare products Regulatory Agency's yellow card scheme. All ADRs identified in a study of hospital inpatients were graded for severity according to the NPSA scheme and the yellow card scheme. ADRs occurred in 15 per cent of patient episodes but reporting of ADRs according to NPSA guidance seemed to offer little

additional value in efforts to improve patient safety over and above the yellow card scheme. The authors suggested that the availability of more than one system could confuse ADR reporters.

**McLernon** (University of Aberdeen) *et al* found differences between yellow card reports submitted by patients and healthcare professionals. In this study of 26,129 yellow card reports patients reported more reactions per yellow card report (three versus two), more reactions involving the nervous system (40.5 per cent versus 20.4 per cent), general reactions (38.4 per cent versus 22.9 per cent) and gastrointestinal disorders (32.5 per cent versus 19.5 per cent). However, fewer of the reactions reported by patients resulted in serious events.

ADRs are known to be a cause of hospital admission, but little is known about their influence on hospital readmission. In a further study by **Davies et al**, ADRs were found to be a significant — but potentially avoidable — cause of hospital readmission. One fifth of patients in this study were readmitted to hospital within one year of discharge due to an ADR. The most frequent drugs responsible for ADRs were antiplatelet drugs and loop diuretics, with bleeding or renal impairment the most frequent ADRs. The researchers said that 57 per cent of the ADRs were potentially avoidable.

**Tangiisuran** (Brighton and Sussex Medical School) evaluated the incidence of ADRs in very elderly patients (>80 years old) in hospital, a patient group in whom there have been no recent studies examining this problem. One in seven of the study patients experienced an ADR with three out of four of these reactions being serious and life threatening and a significant proportion preventable. Factors associated with ADRs included the use of six or more medicines, use of hypoglycaemic agents, hyperlipidaemia, raised white cell count and hospital stay of more than five days.

On a more positive note, a drug alert poster improved clinical practice in relation to insulin in 74 per cent of staff in an acute trust, according to a study by **Ledger-Scott** (County Durham and Darlington NHS Acute Trust). The poster was sent by e-mail with a printed copy also sent to each ward for display. This method of dissemination worked particularly well for pharmacists and nurses, but only 65 per cent of junior doctors had read the alert compared with all the pharmacists and 98 per cent of the nursing staff.

Poor communication during transfer of patients between hospital wards is a root cause of patients missing doses of medication in hospitals. This finding emerged from a study by **Sedgwick** (County Durham and Darlington Foundation Trust) *et al*. Of the 73 patients included in the study, 32 missed at least one dose of medication despite it being available on the ward. Missed doses included insulin, Parkinson's disease drugs and antibiotics.

Continuing with the importance of communication on medicines as patients move settings, **Terry** (Department of Pharmacy, Birmingham Children's Hospital) *et al* found that the introduction of medicines reconciliation in children is likely to reduce medication-related harm, mirroring similar findings in adults. This study involved 100 children admitted to a paediatric neurosurgical ward. Medicines reconciliation performed by a pharmacist identified 38 disparities in 22 children between the initial hospital prescription and the medication prescribed before admission.

### Learning and development

Our schools of pharmacy continue to develop new methods of teaching and learning. Robert Gordon University has recently begun to combine face-to-face with electronic instruction for teaching pharmaceutical public health. **Diack** (The Robert Gordon University, Aberdeen) *et al* have developed a module in which internal staff, tutors and students work together online in groups of 10 to 12 to complete directed study, coursework and assessment. Students are encouraged to develop their own public health practice by creating a service development bid. Student engagement, analysed using online tracking tools and course evaluation tools, was found to be exceptional.

Many of us learn well by doing, which was confirmed in a study by **Apampa** (Medway School of Pharmacy, Kent) *et al* who surveyed second-year undergraduates and graduates of Medway School of Pharmacy to ask them what they thought about learning in a community pharmacy under the supervision of an instructor. Results suggested that students valued their early practice experience in a community pharmacy while studying for their degree. They said it helped them to develop their professional skills and attitudes, which as the authors state, is important at a time when the profession is taking on a more patient-focused approach.

Leadership skills are essential to support the profession through these times of huge change. **Lambat** (Welsh School of Pharmacy, Cardiff University) *et al* explored the views and experiences of 18 participants in the Pharmacy Leadership Programme for Wales. This programme consisted of two national two-day workshops and up to eight regional action learning sets (ALSs). The aim of the ALSs was to identify learning needs and provide a vehicle for resolving leadership dilemmas. The ALS format was found to be a powerful tool for personal development and individuals were already making changes to their professional practice as a result of the programme.

Turning to the learning of registered pharmacy technicians, a study by **Schafheutle** (University of Manchester) *et al* found that a Centre for Pharmacy Postgraduate Education (CPPE) workshop on influencing skills for pharmacy technicians resulted in positive



Pharmacists are struggling to cope with increased workloads

learning outcomes. Over half of the 122 respondents who gave detailed feedback on the course explained how they had introduced, changed or improved a system within their workplace. Some said the knowledge gained at the workshop had helped them gain a new job or additional responsibilities while others commented on how the workshop had helped them to make a case for new equipment or to improve communication within the pharmacy team.

### Workforce issues

It will come as no surprise to *PJ* readers that changes in pharmacy have increased professional workload. **Ferguson** (University of Manchester) *et al* interviewed 26 pharmacists and found that all of them were struggling to cope with increased volumes of work, staff shortage and deteriorating work conditions, all of which compromised their job satisfaction.

In another study from Manchester, **Seston and Hassell** found that community pharmacists seemed to experience more difficulty

balancing work and home commitments compared with hospital pharmacists, while men experienced greater problems with work-life balance than women.

**Willis** (University of Manchester) *et al* found that career commitment was higher among white women than among any other groups in the study and was noticeably lower among men from minority ethnic groups. Those who felt satisfied with, and in control at, work and those who saw good career development opportunities in the future were also more likely to feel committed to working as a pharmacist.

Does an accredited checking technician (ACT) improve work-related stress? The answer seemed to be "no" according to a study by **McCann** (Queen's University, Belfast) *et al*. Although the six surveyed pharmacists believed that an ACT was a valuable member of the pharmacy team with the potential to free pharmacy time, most said that they were ultimately responsible for checking and the cost of ACT training did not produce sufficient benefits.

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# Science Chairman's address: nanomedicines in sharp focus

Ijeoma Uchegbu describes how nanoparticles can be used advantageously to alter drug biodistribution and unlock the potential of various compounds

**D**rug delivery is a fairly new discipline, although the compounding of medicines to facilitate drug administration is a reasonably well established field of endeavour. However, controlling the distribution of drug compounds after they have been administered is probably a “teenage” science — still uncontrolled yet full of promise.

If drug biodistribution could be controlled absolutely there would be minimal side effects and greater compliance. More importantly, drug compounds that at the moment cannot be used because they are unable to get to the site of action, could be. This class of compounds includes genes, promising therapeutics stalled by a lack of delivery options, peptides and high molecular weight pharmacologically active agents with central nervous system activity that cannot get into the brain, and poorly soluble drugs that are not absorbed in sufficient quantities to guarantee activity.

In our laboratory we use nanoparticles to attempt to alter advantageously drug biodistribution and hence unlock the potential of various compounds (see Figure 1). Our tools are polymers, which are large molecules sometimes a thousand or more times higher in molecular weight than aspirin.

A key feature of our laboratory is the engineering of particles. Self assembly is the process by which polymers are turned into particles and is directed by the polymer's chemistry. We focus on making sure that particles have the right morphology (see Figure 2) — particles may be hollow or filled — and on making sure that particles are able to encapsulate the drugs that we want to deliver. Our activities are also geared towards getting the size of the particles right since particle size influences drug biodistribution, for example, particles smaller than 400nm are better at delivering drugs to the brain. We have



Craig Strong

Ijeoma Uchegbu addresses the conference

found that polymer molecular weight impacts directly on particle size and have exploited this to produce optimum sized particles.

A further area of activity is constructing drug particle formulations that are stable for prolonged periods — up to nine months — and producing particles of various shapes, since this, too, can influence drug delivery.

We have also constructed particles that have a very high drug load, with up to 45

per cent of the particle being the drug. This high drug load is useful because it allows formulators to work with less of the polymer excipient. It is especially helpful for delivering medicines required in high doses.

Once functional nanoparticles such as ours have been loaded with drugs they are known as nanomedicines, simply because the nanotechnology is enabling.

## Conference Science Chairman

Ijeoma Uchegbu occupies the chair of pharmaceutical nanoscience and is director of postgraduate research studies within the department of pharmaceuticals at the School of Pharmacy, University of London. She was previously professor of drug delivery at the School of Pharmacy, University of Strathclyde, Glasgow.

Her research is concerned with the design, synthesis and use of amphiphilic polymers and low molecular weight dendrimers to effect drug and gene delivery solutions.

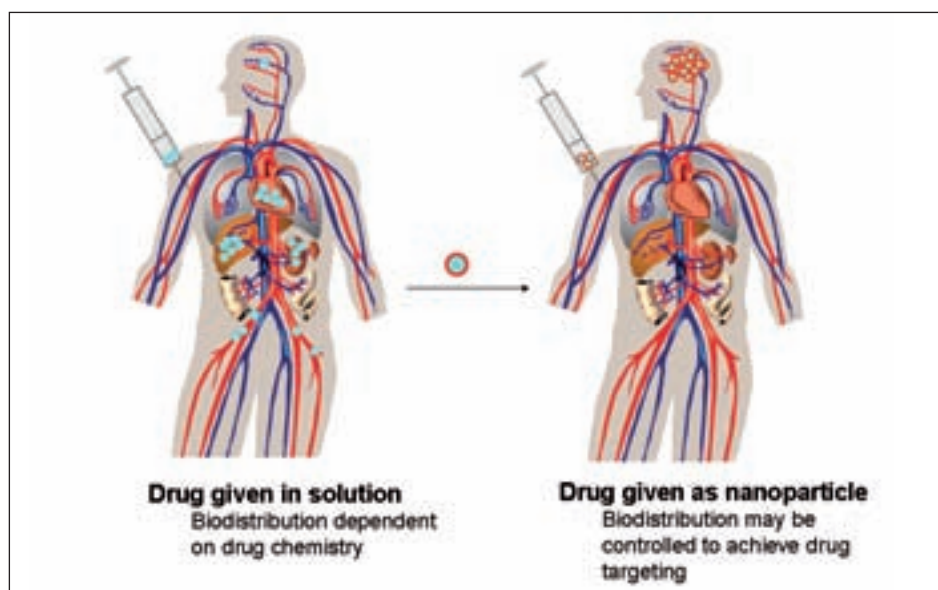
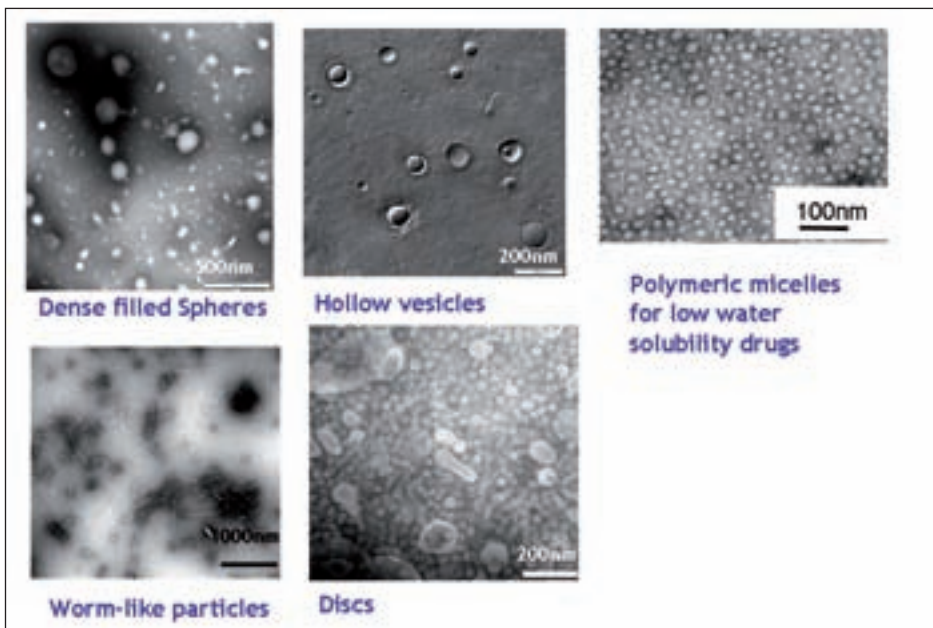
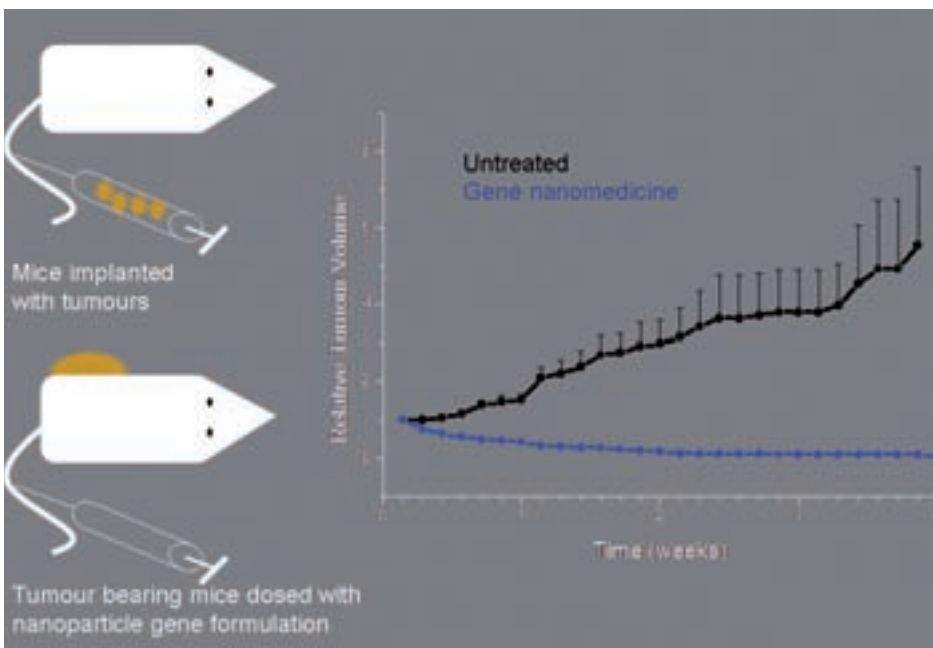


Figure 1: Nanoparticles can advantageously alter drug biodistribution



**Figure 2: Particle structure can influence drug delivery**



**Figure 3: Nanoparticles allow the gene to enter the cell and reduce the tumour**

So what can these particles do for pharmacy? In the case of drugs with poor water solubility, these nanomedicines promote drug absorption via the oral route, producing a formulation that results in a three-fold increase in drug absorption. This was demonstrated with ciclosporin A as a model drug and in preclinical studies in rats.

Our nanomedicines also promote drug delivery to the brain. Delivery of drugs to the brain is limited because the brain is protected by the blood-brain barrier: a barrier of tight blood vessel cells that do not allow most molecules to cross. This keeps the brain healthy but it often limits the amount of drug that can access a diseased part of the brain. By using our nanomedicines, we have been able to increase the activity of drugs in the brain by up to 10-fold, and this was demonstrated using propofol in a mouse sleep model.

A final area of success with this nanotechnology is gene therapy in preclinical cancer models. Genes and ribonucleic acid sequences could be used to treat cancers if only they could be successfully delivered. Tumouricidal genes which result in tumouricidal proteins have been shown by us to result in complete tumour shrinkage once the genes are packaged into our nanoparticles. The nanoparticles ensure that the gene is not destroyed by plasma enzymes and is able to enter the cell to produce the protein. In our studies, which were conducted in tumour-bearing mice, the protein was tumour necrosis factor- $\alpha$ , which, on being produced in the cell, caused tumour shrinkage (see Figure 3).

In summary, nanoparticle engineering has resulted in nanomedicines that significantly improve the pharmacological activity of phar-

macologically active molecules that pose a problem for pharmaceutical development, such as various hydrophobic drugs and genes.

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# Debate: are medicines too expensive?

Who is to blame when the high cost of medicines prevents patients from receiving optimal treatment? This issue was debated by a speaker from Oxfam and one from The School of Pharmacy, University of London, during a BPC 2009 science session. **Gareth Malson** reports

The high price of medicines is caused by greed on the part of the pharmaceutical industry, said Mogha Kamal-Yanni, senior health and HIV adviser for Oxfam. She was speaking in support of the motion: "This house believes that medicines are too expensive."

Dr Kamal-Yanni believes the core argument for the industry charging a high price — to recoup the vast cost of research and development — does not tell the whole story. For example, she highlighted research that estimated the cost of getting a new medicine onto the market to be around \$1.3bn. "Is the cost that high," she asked. "This figure is based on one study — funded by [the industry] so for a start we've got conflict of interest."

"The data are not available to anyone. We can't examine [the data], we just have to believe it." She went on to suggest that this figure incorporates marketing costs and the assumption that if the manufacturer had not spent money on research, it would otherwise have invested it in something else and made a healthy return. She also pointed out that the tax allowances that become available as a result of investing in research were not considered in this amount.

## R&D is expensive

Arguing against the motion, David Taylor, professor of pharmaceutical and public health policy at The School of Pharmacy, University of London, said there was no point quibbling over the exact cost of research. "Is research and all the things you do to get the drug on the market expensive? Yes," he said. "The cost of producing it once you get there is often low . . . but what is a fair price?"

"Do you charge the moderate cost of production — the idealised generic price — or do you charge a price that, over a given period, is intended to give you a return on investment and an incentive to go on investing?" He went on: "Investing in things that are reasonably safe, like, hopefully, houses, is very different from investing in things that are really hazardous."

Dr Kamal-Yanni criticised the practice of developing "me-too" drugs and questioned whether it was innovative to tinker with existing drugs just to create new ones in the same class.

She pointed out that, during the past few years, only about 15 per cent of the medicines approved by the US Food and Drug Administration were better therapeutic options than what was already on the market. Furthermore, she highlighted that the cost of research for such me-too drugs was



**Mogha Kamal-Yanni: blockbuster model no longer working**

unlikely to be as great as the research costs for "innovative" medicines.

## End of the blockbuster era

Dr Kamal-Yanni said that the "blockbuster model", by which many pharmaceutical companies had operated for many years, was no longer working. Furthermore, because there were no new blockbusters in the pipeline, pharmaceutical companies were employing different tactics to protect their bank balances. These included vigorous protection of patent, expansion into new markets for which only small numbers of people could access expensive treatments, more expenditure on marketing and increased drug prices. Consequently, she believed the industry was failing to honour its "social contract".

Professor Taylor disagreed: "I genuinely believe the pharmaceutical industry to be one of the more successful institutions in human society . . . its contributions are useful."

He concurred that the blockbuster era was over, but argued that it was because there were few blockbusters left to discover, not because manufacturers had stopped trying to discover them. In addition, when a company does invent an innovative product it is often only suitable for small numbers of people. This, along with the fact that generic prices were so low, meant that the cost of new drugs had to be much higher, he said.

He also pointed out that government funding for research often follows private profit. So, funding for research is unlikely to be forthcoming unless it expects to yield profit for private companies.

## A higher cause

Professor Taylor decreed that solving world health problems should be the focus of everyone's efforts. "Personally, I would extend pharmaceutical product patent lives considerably . . . in return for guarantees of world supply to all populations."

Dr Kamal-Yanni responded by suggesting that extending patent licences would be "a disaster" because it would prevent generic competition from forcing prices down and would just mean it took longer for the price to drop to a level that developing countries could afford.

She believes it is unfair that healthcare workers, particularly those in developing countries, are put in a position where they need to decide who is treated and who is not — therefore potentially who lives and who dies. "I've done that before, I wouldn't want to do it again," she said.



**David Taylor: cost of new drugs has to be high**

# Temozolomide: a pharmacist's tale

The discovery of anticancer drug temozolomide and its turbulent journey to market was described by Malcolm Stevens, emeritus professor, University of Nottingham, and chief scientific officer, Pharminox, during the Academy of Pharmaceutical Sciences annual award lecture. **Harriet Adcock** reports

Mitozolomide (Azolastone) became an example of what not to do in anticancer drug discovery, Malcolm Stevens, emeritus professor at the University of Nottingham and chief scientific officer at Pharminox, told conference participants during the Academy of Pharmaceutical Sciences annual award lecture. Professor Stevens described how his research group at Aston University worked on the development of mitozolomide in the 1970s, where he had funding to synthesise pharmaceutically interesting molecules.

The group, which included several pharmacists (many of whom have gone on to hold distinguished positions in the field of drug development), developed six molecules that were taken into clinical trials, two of which found their way to market. This was all achieved over 20 years at a cost of less than £10m, said Professor Stevens.

"We were successful because we had expertise spanning chemistry, supplemented with lots of PhD students and undergraduate projects, we had pharmacologists, toxicologists and a pharmaceutical development pharmacist," he explained.

Mitozolomide was rapidly taken into the clinic after being found to clear lymphoma from mice using a single dose, but proved to be disastrous, said Professor Stevens. "It was disastrous clinically and disastrous politically," he said. In trials, its antitumour effects were not observed and it showed unpredictable thrombocytopenia. "This spelt the end of mitozolomide," said Professor Stevens, who at this point developed a personal strategy for discovering molecules that were easy to synthesise and named it "molecule whispering".

Professor Stevens' approach to drug development was simple — all compounds put into clinical trials had to be easy to synthesise, for example, using a two-step process, and only 50 to 60 molecules in any class would be synthesised. Molecules taken forward needed to interfere with a novel biological mechanism and had to have robust pharmaceutical properties.

"The art is getting these three processes working together over a programme of synthesising 50 to 60 molecules," he said. "If you can't do it within those molecules, you're unlikely to do it in 5,000 or 50,000 molecules," he said.

He added that another feature of molecule whispering was that, to be successful, researchers must be prepared to "fall in love" with the molecules they are working with.

Following the ill-fated mitozolomide, Professor Stevens' group used his molecule whispering strategy to develop other compounds. Among them was temozolomide —



**Malcolm Stevens developed a personal strategy for discovering molecules**

a simpler molecule than mitozolomide, without DNA cross-linking capability.

The reaction used to synthesise temozolomide — known as the Stone reaction — was a one-pot reaction, with cheap starting materials and a high yield. However, at the time the research group wanted to take synthesis of temozolomide forward, the Bhopal disaster happened in India, Professor Stevens reported. The culprit molecule in the Bhopal disaster was methyl isocyanate, required to make temozolomide via the Stone reaction. "We got diverted looking for different ways of making it — but none was as good and the drug is still made commercially by this process," he added.

Temozolomide's antitumour properties were explored and the molecule put into clinical trials, where it produced some extraordinary results, said Professor Stevens. Most remarkably of all, a series of patients with brain tumours experienced a major clinical response.

"Cancer Research UK went out on the road to show temozolomide to various pharmaceutical companies. Sadly, there were no British companies that were interested — they thought it was too risky to synthesise." However, temozolomide was eventually licensed to Schering Plough and marketed in 1999.

Further work was carried out to explore the drug's mechanism of action. By putting various isotopes into temozolomide —  $^{15}\text{N}$ ,  $^{11}\text{C}$  and  $^{14}\text{C}$  — it was possible to account for what happens to all the atoms in the molecule.

"Critically, using  $^{11}\text{C}$  isotope we could show that the carbon is expired as  $\text{CO}_2$  gas,

leaving a methyl group doing the business. . . . So we know precisely what happens to the molecule — its ring opens and then undergoes a cascade of degradation, eventually generating a very short-lived reactive methyl diazonium ion that methylates the guanine base in DNA."

The methylated guanine hydrogen bonds to thiamine resulting in a so-called DNA mismatch, which then alerts the mismatch repair machinery of the cell. "We now know that the success or failure of temozolomide in patients depends on the presence or absence of a DNA repair protein — MGMT — methyl guanine methyl transferase. . . . Patients whose tumours are proficient in MGMT can reverse the repair and so respond poorly," explained Professor Stevens.

Further along temozolomide's journey, the National Institute for Health and Clinical Excellence came down hard on the drug and originally would not approve it for reimbursement. This caused great concern to some of the clinicians involved in its development, who were unable to prescribe it on the NHS, said Professor Stevens. However, it proved to be a wonderful example of translational research, he said, adding that the drug sold over \$1bn in 2008.

Asked if he would do it all again, Professor Stevens said that he would recommend pharmacy as a career for anyone interested in science. "It gives you all the options — of being a microbiologist, a chemist, a physiologist and disciplines that did not exist when I was a student, such as tissue engineer and nanotechnologist. There are pharmacists making major impacts in all these areas and I would certainly do it all again," Professor Stevens concluded.

# Pursuing effective anti-infectives

The emergence of drug-resistant infectious diseases is being met with a dearth of new anti-infective medicines — but there are new treatment options to be explored. **Francesca Rivers** reports

Resistance is a recurring challenge in the battle against infections, limiting the lifetime of a drug and providing a constant need for new drug targets. Meanwhile the drugs pipeline has dried to a trickle, with high research and development costs and approval issues holding back a much-needed drive for new treatments. Such was the message from many of the speakers on infectious diseases and anti-infective medicines at this year's British Pharmaceutical Conference.

## Drug resistance

We have created some monsters through the overuse and misuse of antibiotics, the conference heard. Rachel McKendry, of the London Centre for Nanotechnology at University College London, argued that unless new discoveries are made, the burgeoning problem of multi-drug resistance threatens to return us to the pre-antibiotics era.

Professor McKendry described a new method for assaying microbial resistance to antibiotics, using nanomechanical cantilever sensors to study reactions and assess bactericidal activity. Her research team recently received two grants to progress their work further. A £2m grant from the Engineering and Physical Sciences Research Council will go towards developing a hand-held system for metacillin-resistant *Staphylococcus aureus* testing, while the second project will see them producing nanosensors for both MRSA and HIV.

## New therapeutic directions

Peter Taylor, of the School of Pharmacy, University of London, argued that there is not enough investment in, or teaching about, infectious diseases in schools of pharmacy in the UK.

The pharmaceutical industry is also no longer investing heavily in antibacterial chemotherapy, focusing instead on more profitable areas, such as chronic and lifestyle-related diseases, he added. "Things are shifting now, but it may be a little bit too late," he warned, stressing that new partnerships need to be developed to address the pressing need for new therapeutic agents.

Alternatives to conventional antibiotic chemotherapy are required, Professor Taylor told participants.

Conventional antibiotics have single biochemical targets, giving bacteria the opportunity to circumvent the action of the antibiotic via discrete changes to its cellular biochemistry. Agents that inactivate or disable the bacteria through modification of the bacterial phenotype may be preferable, he argued, citing photosensitive bacterial inactivation and

bacteriophage-derived enzyme therapy as approaches currently being investigated.

Professor Taylor's research group has identified a specific enzyme that can alter the course of systemic infection with neonatal bacterial meningitis by removing the protective poly-sialic acid capsule expressed on the surface of most of the pathogenic strains of *Escherichia coli*.

"[The sialic acid is] actually a host antigen that is expressed during embryonic development, and the bacteria mimic this to escape detection by the immune system," said Professor Taylor, explaining that the enzyme they have identified is specific to the bacterial capsule and does not attack the host cells.

Studies using a rat model of neonatal bacterial meningitis have demonstrated that direct administration of the enzyme into the intraperitoneal cavity can cure or prevent infection and almost eliminate brain inflammation in 90–100 per cent of the animals. "This demonstrates that the idea of modifying the phenotype at the site of the infection will work," said Professor Taylor.

His group is also investigating compounds that modify bacterial resistance, such as catechin gallates, compounds found in green tea that have been shown to modify the beta-lactam susceptibility of MRSA.

## Immunotherapy

Immunotherapy was proposed by Gregg Sando, founder and chief executive officer of cellular therapeutics company Cell Medica, as another alternative to antibiotics for the treatment of viral infections. Cell Medica research has explored the possibility of using cell-based immunotherapy to treat cytomegalovirus in immunocompromised patients whose weakened immune systems leave them vulnerable to reactivation of latent infections.

Approved for routine use in the UK by the Medicines and Healthcare products Regulatory Agency, the therapy is given to bone marrow transplant patients via a blood infusion.

Phase I and II trials have demonstrated successful protection against cytomegalovirus, with no significant side effects, but graft versus host disease has proved a key complication to the treatment. A clinical trial is currently under way in 13 hospitals across the UK in order to develop a reimbursement case to present to the NHS, explained Mr Sando.

T-cell immunotherapy has been under active development for around 20 years now and we will see it emerge into clinical use, he predicted. The therapy has potential for use in the treatment of autoimmune disease, as well as preventing certain cancers that are related to immune system dysfunction, such as cervical cancer and human papilloma virus, he said. Cocktail treatments that would target more than one infection at a time are also a likely progression, he added.

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# Steroid sulphatase inhibitors: pushing the frontiers of cancer research

Discovery of a new class of anticancer agents saw professors Barry Potter and the late Michael Reed awarded the 2009 GlaxoSmithKline Industrial Achievement Award. Accepting the award, Professor Potter detailed the development of the new agents. **Francesca Rivers** reports

The traditional approach to treating cancer using cytotoxic therapies that simply interfere with rapidly dividing cells is giving way to the concept of targeted therapy, whereby cancer cell growth is blocked via interference with specific molecules involved in the disease pathway, said Barry Potter, professor and head of medicinal and biological chemistry at the University of Bath.

At this year's British Pharmaceutical Conference, Professor Potter accepted the 2009 GlaxoSmithKline Industrial Achievement Award on behalf of himself and his late research partner Michael Reed, professor of steroid biochemistry at Imperial College, London. The award was given for their involvement in the discovery of steroid sulphatase inhibitors — which are currently in clinical trials and promise to emerge as a new class of anticancer drugs in the near future. In a lecture mapping the development of the compounds, Professor Potter said the search for new therapeutic targets for cancer is progressing.

Research into new treatments for hormone-dependent breast cancer focuses on finding compounds that can interfere with oestrogens (particularly  $17\beta$ -oestradiol), steroid hormones that play a part in carcinogenesis via the activation of transcription. Tamoxifen, which works by blocking the binding of oestradiol to its receptor, has been the gold standard treatment for years, said Professor Potter, but his research group came to the conclusion that they needed to adopt a different approach, based on controlling the levels of these hormones within the tumours themselves. "Our aim was to try to define a new type of endocrine therapy that would block the effects of oestrogen on tumour cell proliferation," he explained.

## Interrupting oestradiol production

The current dogma is that the aromatase enzyme — which converts androstenedione to oestrone, which is subsequently converted to oestradiol — is a good drug target, a theory that has been borne out in the clinic for several years, said Professor Potter. The blockbuster drugs anastrozole and letrozole exert their effect through aromatase inhibition and are becoming the new gold-standard in anti-endocrine therapy, in some cases supplanting the use of tamoxifen as first-line therapy, he observed.

But a large amount of oestrone is produced in cancer cells by the action of oes-

trone sulphatase, a steroid sulphatase (STS) that thereby provides a source of oestradiol that cannot be blocked by an aromatase inhibitor. Another steroid, androstenediol, is also active at the oestradiol receptor and produced through an aromatase-independent (but sulphatase-dependent) pathway. Both of these pathways are exciting targets for a new therapeutic approach, he said.

Unlike aromatases, STSs are expressed by all breast tumours and are easy to detect in the cytoplasm of carcinoma cells. High levels of STS often correlate with a worse prognosis for breast cancer patients, making STS inhibition a good target for the treatment of cancer. Professor Potter and his team carried out structure-based design work to produce a series of compounds that were structurally similar to the STS substrate oestrone sulphate, and tested their ability to inhibit the enzyme.

A steroidal sulphamate ester, oestrone 3-O-sulphamate (EMATE), emerged as an effective time- and concentration-dependent inhibitor of STS. EMATE was found to be unsuitable for development as an anticancer drug, but has been taken forward into phase I and II clinical trials as a candidate prodrug for hormone replacement therapy. Meanwhile, the group produced a series of similar but non-steroidal sulphamates and studied their effects on STS activity, leading to the identification of a lead drug candidate: STX64.

## STX64

As well as being an easy compound to synthesise, STX64 has been shown in *in vivo* trials in mice to be highly potent and non-oestrogenic, with a high oral bioavailability. An important feature of the compound is that it is sequestered into red blood cells following oral administration, and thus avoids primary metabolism and emerges later to exert its pharmacological action.

Professors Potter and Reed founded a Bath and Imperial College University spin-off company called Sterix in order to take the promising compound forward into "first-in-class" clinical trials, with the main objectives of establishing a toxicity profile for the drug and discovering the oral dose required.

A dual-centre phase I trial involving 14 postmenopausal breast cancer patients administered either 5mg (nine patients) or 20mg (five patients) doses of STX64 produced exciting results, recalled Professor Potter. The



Barry Potter accepting the award

drug was well tolerated and could produce complete inhibition of STS. Interestingly, and surprisingly, said Professor Potter, the drug did not just produce a decrease in STS activity but also reduced levels of the steroid serum androstenedione, which is a substrate for the aromatase enzyme. Five patients who had previously shown disease progression, including on aromatase inhibitor therapy, had clinical evidence of stable disease after treatment with STX64.

Three further clinical trials of reformulated STX64 are currently under way in France, Belgium and the UK under the auspices of the pharmaceutical company Ipsen. "We hope to see results coming through shortly," said Professor Potter.

## Other applications

STS inhibitors also have the potential to treat other diseases that have a hormonal element, such as endometriosis, endometrial cancer and androgen-dependent prostate cancer, explained Professor Potter. Clinical trials of STS inhibitors for some of these indications are currently under way.

Nadia Attura

Hormone-independent tumours are more challenging than their hormone-dependent counterparts, explained Professor Potter, and his new streams of work include finding and developing anticancer compounds that work independently of STS-inhibition — such as microtubule disruptors and anti-angiogenic agents — for the treatment of hormone-independent cancers. STX140 is one such orally active drug candidate, which is delivered by the blood transport system and has demonstrated anti-proliferative and anti-angiogenic action, with profound effects on tumour vasculature. Both STX140 and a fellow candidate STX243 have produced exciting results in trials with murine models of androgen receptor negative prostate cancer.

Recent press coverage of the group's work on a potential treatment for hormone-

independent breast cancer has grossly exaggerated some of the progress that has been made, commented Professor Potter. He said that while it is good for the work to have exposure, it is not desirable for patients to believe a new pill is available when the compound has not even yet progressed into clinical trials.

He added: "We're very hopeful this drug will go further, and will be very successful in at least one of the indications. If it does, it will be . . . proof that you can take compounds from the university bench way beyond what you might have imagined would be dreamable."

The labours of Professor Potter and his research group have led to the development and patenting of a first-in-class aryl sulphamate pharmacophore, which he hopes will

prove applicable in many disease areas and allow the design of drugs in addition to those that have already entered clinical trials.

A stronger focus on drug discovery is needed in academia in order to plug the innovation gap that has formed, said Professor Potter, observing that the pharmaceutical industry has invested enormous amounts of money in drug discovery over the past decade, with a diminishing output of compounds submitted for approval.

"I feel personally that we should be engaging far more, in the academic community, with our industrial colleagues, to think up new ideas for [drug] discovery," he said. "We need much more use of the good minds in universities, to apply them in a sensible fashion to drug discovery."

# Growth of pharmaceutical industry in current economic climate questionable

Personalised medicines, and disease modification and prevention, represent opportunities for the pharmaceutical industry. **Nicola Cree** reports

There are a number of challenges facing the pharmaceutical industry, Brent Vose, vice-president, global drug development, AstraZeneca, told the conference.

Whether growth of the industry will continue in the current economic climate is questionable, he said, adding that growth had already slowed in the US, UK and Japan, leaving the industry to rely on emerging markets.

In the past 10 years sales of pharmaceuticals have increased 160 per cent, Mr Vose said. Research and development (R&D) expenditure has increased by 80 per cent, but productivity — measured by the number of new medical entities to be approved — has decreased by 43 per cent. "We're putting more money in, it's taking us longer and we're getting less out," he said.

To bring one drug to market it is estimated that it costs over \$897m. It takes 12 years to develop a new medicine but 80 per cent of drugs do not show a positive return on investment, leaving only 20 per cent to fund the R&D engine, said Mr Vose. Pricing pressures, the impact of the National Institute for Health and Clinical Excellence and patent expiry leaving very little time to recoup R&D costs, are all challenges the industry faces, said Mr Vose.

## Opportunities

There are a number of opportunities for the industry, added Mr Vose. It is important to try to move away from symptomatic treatment to disease modification and prevention. It is also important to move towards personalised medicines, he said, adding that AstraZeneca



**Brent Vose: try to move away from symptomatic treatment**

estimates that over time, 50 per cent of its portfolio will have associated with it a patient segmentation tool. Part of AstraZeneca's R&D operating model is to look at whether there is a patient segmentation opportunity for each target it takes on board. The company is also looking to work with providers of diagnostics.

"Predictive science and personalised healthcare are . . . an approach to thinking

about attrition," said Mr Vose. There needs to be greater disease understanding so that treatments are interfering with disease mechanisms in an effective way, he said. Predictive science will help ensure the safety of medicines, and improve efficacy and success rate.

Biologics and genetics also offer an opportunity to the industry, he added. There are fewer toxicology issues with biologics, he said.

The development of emerging markets is an opportunity for the industry and it leads to the question "Should the industry pursue different disease targets in different locations?", said Mr Vose. Examination of cancer specimens in China has shown that diseases are different in different locations, he said, adding: "It is fantastically important for us to stop this UK-centric, or Western-centric, view of the world and start to reach out and address these other problems."

## Design strategy

When talking about how AstraZeneca aims to improve its design strategy, Mr Vose told participants: "The world of science is changing and is changing faster and faster, and if you don't stay with it, you will certainly be left behind."

A large part of the development of drugs is satisfying regulatory bodies, said Mr Vose. Patients, regulatory bodies and NICE may have different demands, and it is important to know what those demands are and to satisfy them — "otherwise you will be in the 80 per cent that don't make a return on investment", he said.

# Methylene blue for Alzheimer's disease

The serendipitous discovery that methylene blue may be an effective treatment for Alzheimer's disease was described by John Storey, senior lecturer, University of Aberdeen, in a session on the search for novel drugs. **Nicola Cree** reports

**M**ethylene blue may be the next treatment for Alzheimer's disease, according to John Storey, senior lecturer, University of Aberdeen.

The serendipitous discovery by Dr Storey's team of methylene blue as a treatment for the condition has led to phase II trials.

Dr Storey explained that it is now believed that the effects of Alzheimer's disease are caused by neurofibrillary tangles caused by tau protein in the brains of those suffering from the disease. There are two ways to deal with the tangles — stop the formation, or devise a mechanism to break down the tangles, Dr Storey said.

When staining slide samples of the tangles, Dr Storey's team discovered that methylene blue degraded the tangle. His team has since worked to develop a pure formulation of methylene blue that can be taken orally, he explained.

In the phase II trials, there was a slight improvement in symptoms in the first 12 weeks of treatment, and in some patients there was a dramatic improvement, said Dr Storey. Following treatment patients did not regress and progression of the disease was halted in over 80 per cent of the patients over 102

weeks, Dr Storey said. The 60mg dose ADAS-cog score (Alzheimer's Disease Assessment Scale-cognitive subscale) at 84 weeks was not significantly different from baseline ( $P=0.216$ ). A dose of 60mg three times a day appears to be the minimum effective disease-modifying dose which also has an acceptable benefit/risk profile, said Dr Storey. The efficacy is supported by molecular brain imaging, Dr Storey added.

Side effects of the drug include blue urine, which Dr Storey admits can be a problem to those suffering incontinence, and bright blue diarrhoea, which occurs at 12 weeks.

Methylene blue treats Alzheimer's progression from an early stage, a stage that is difficult to detect by psychologists, Dr Storey said. However, his team has developed a diagnostic ligand, detected by a positron emission tomography scan, designed to detect Alzheimer's disease at the earlier stage, he added.

## Combining therapies

It is difficult to find new drug targets and therefore thought should be given to combining therapies, said Gavin Whitlock, associate research fellow, Pfizer global research

and development. It is a challenge, however, to combine more than two pharmacological activities in a human while maintaining a sufficient safety window — it is critical to understand the *in vitro* and *in vivo* correlation and the potential for drug-drug interactions and pharmacokinetic, pharmacodynamic and formulation incompatibilities, he added.

There are three ways this can be done, Dr Whitlock explained. Two active compounds can be conjugated with a linker, where there are structural similarities in the two types of ligands two pharmacophores can be integrated using a ligand overlap, and there is also a fused approach — optimising a structure that already has both the activities that you are looking for.

The conjugated approach is successful for non-oral molecules because the molecules are fairly large. The integrated approach is better for oral drugs, Dr Whitlock said.

Going forward, Dr Whitlock said, it is important to understand what the key safety risks of pulling two or more pharmacological activities together are. There is a long way to go with regards to methods of validating the biological approaches, Dr Whitlock added.

## New professional body: the future is orange!



Sharon Hart (left), NHS Connecting for Health, in conversation with Heidi Wright, head of practice, Royal Pharmaceutical Society, at the new professional body stand

Craig Strong

# Thinking differently to drive innovation

Two speakers described how pharmaceutical companies are protecting their revenues through innovation. **Harriet Adcock** reports

Enhanced product development was the theme of a talk given by Andy Lewis, director of operations for Critical Pharmaceuticals.

Dr Lewis pointed out that enhanced biopharmaceutical products allow companies to protect their revenues, given the limited life of patents and the costs of getting new products to market.

He described some of the techniques that have been used to try to deliver human growth hormone (hGH), a therapy traditionally administered via injection because of its propensity to aggregate. Techniques have included sustained release formulations and pegylation in order to prolong the activity of the therapy and reduce the need for frequent injections.

One sustained release growth hormone product that got to market was Nutropin depot, Dr Lewis said. However, it was withdrawn due to poor manufacturing efficiency. Hormone levels were also found to drop below therapeutic levels so children had to be given multiple injections.

Most of the companies marketing hGH have attempted to use molecule modification, such as pegylation, to enhance their formulations, said Dr Lewis. However, attempts have generally been abandoned due to problems with increased toxicity and loss of activity.

The need for enhanced formulations remains, Dr Lewis suggested, pointing out that in a recent survey, 70 per cent of children or their carers reported that they do not like having to inject hGH on a daily basis, with 30 per cent considering halting treatment. "If we can develop products that make it easier for children to take their growth hormone or at least make it less unpleasant then there is the potential to increase efficiency and reduce healthcare costs," he said.

Dr Lewis went on to describe the development of two technologies that can be applied to enhanced biopharmaceutical products — CriticalMix and CriticalSorb.

CriticalMix uses supercritical CO<sub>2</sub> to encapsulate drugs into polymers. Drug and polymer are added to the manufacturing chamber as solids, with CO<sub>2</sub> pumped in and the temperature increased to 32C until the CO<sub>2</sub> becomes supercritical. At this point, explained Dr Lewis, the polymer liquefies and the drug remains solid. The components are mixed then expelled from the chamber via atomisation producing microparticles.

The advantages of the CriticalMix process is that it avoids some of the issues that hinder other encapsulation technologies, said Dr Lewis — it is a dry process with no shear stresses and no organic solvents, and the process works at an ambient temperature so there are no concerns about the protein denaturing.



**Andy Lewis described new technologies for delivering growth hormone**

The process has successfully been used with hGH and 20 to 30 other proteins and peptides, said Dr Lewis. The proteins retain their activity and structure and the microparticles produced are injectable through fairly small needles (for example, 25 gauge needles). There is a high encapsulation efficiency and,

since it is a single step process, drug is not lost through extraction procedures.

The hGH formulation has been tested in non-human primates and plasma levels are sustained for at least seven days, reported Dr Lewis. "We think that such formulations will be injected every two weeks."

Turning to CriticalSorb, Dr Lewis explained that, although he could not reveal exactly what the technology involves, it is a marketed pharmaceutical excipient used as a solubility enhancer with small molecules and is regarded as safe and non-irritant.

It has been shown with simple formulations to promote nasal absorption of proteins and peptides. And when used to deliver hGH, it results in the highest bioavailability of the protein ever reported for nasal delivery, Dr Lewis claimed.

CriticalSorb is unlike other absorption promoters, said Dr Lewis, which have received a bad press because of their tendency to strip epithelial cells from mucosal membranes. In tests, CriticalSorb was well tolerated after repeated dosing over five days, with no signs of damage to nasal mucosa, he reported.

Dr Lewis's company is currently arranging funding for phase I clinical trials for its growth hormone nasal spray, which will take place in 2010.

## Driving innovation

Steve Wicks, vice-president of pharmaceutical science and technology at Pfizer, gave some insights into how biotechnology and pharmaceutical companies are thinking differently in order to drive innovation and maximise revenue.

Dr Wicks explained that companies try to stack their development programmes so that as generic competition emerges another new product comes to market, producing a sustainable business model. In such an environment, companies can afford to indulge in speculative development. At the moment, however, gaps are appearing in companies' development cycles so industry is becoming more risk averse.

Companies are having to think about other ways to shift their product development cycles. They need to decrease research and development costs, reduce time lines and they need new business models.

Dr Wicks argued that the move into unsustainable cycles is driving innovation — innovation is being seen in the way drug candidate screening is conducted, the types of assays used in testing and in the number of test points that can be completed every day. Automation is providing competitive advantage to maximise the speed of the development process, Dr Wicks explained.

Science is also being applied to maximise efficiency and companies are using more computational models to give them intellectual control over drug candidates, he said.

"We are now in a highly unstable phase, and will be for the next five to 10 years. We have to assure return on investment through exquisitely good pharmaceutical science, done very quickly," Dr Wicks concluded.



**Steve Wicks: industry is becoming more risk averse**

# Vaccine against HIV moves a step closer, according to US researchers

Carl Alving, of the US Walter Reed Army Institute of Research, described recent progress in the development of a prophylactic vaccine against HIV and Nicol Keith, of the University of Glasgow, discussed new targets for cancer treatment. **Francesca Rivers** and **Gareth Malson** report

Until recently the HIV research field has been unable to induce broadly neutralising antibodies by immunisation. Now a research team in the US has accomplished this feat, said Carl Alving, of the Division of Retrovirology at the Walter Reed Army Institute of Research, Maryland, representing a step towards the development of a prophylactic vaccine against HIV.

The challenge is to develop a vaccine that recognises both the 160kD glycoprotein (gp160) that is found on the surface of the HIV cell and the phospholipid bilayer of the cell envelope, explained Dr Alving.

With this objective, his research group created a potential HIV-1 vaccine formulation that included lipid A — a potent adjuvant that can be embedded into liposomes and is already used in the production of a number of vaccines, including the hepatitis B vaccine. A synthetic peptide containing the HIV-binding amino acid sequences of 2F5 and 4E10 (see Panel), which confer gp41-binding specificity, was added to the lipid A liposome formulation. In immunisation trials in mice, the formulation induced production of two mouse monoclonal antibodies, which neutralised HIV-1 and bound both phospholipids

and gp41 (at both the 2F5 and 4E10 binding sites), said Dr Alving.

The use of a vaccine that induces antibodies with phospholipid-binding specificity has raised concerns among the scientific community, noted Dr Alving, because phospholipids are abundant in host cells. "People are worried that if you are to produce antibodies like this it will produce an autoimmune disease, which is quite incorrect," he said. He explained that, although the antibodies produced in this case are autoantibodies, they pose no danger because the lipids of normal human cells are concealed by a layer of protein that the antibody cannot penetrate.

Dr Alving concluded: "We have created highly specific monoclonal antibodies that apparently reproduce the binding sites of 2F5 and 4E10, using an adjuvant liposome formulation that would be suitable for human use." He emphasised that the constituents of the formulation are all well tolerated and relatively inexpensive generic compounds with potential for use as part of a human formulation.

## HIV antibodies for vaccine design

A number of broadly neutralising monoclonal antibodies against HIV have been obtained in the past from blood samples taken from infected individuals, explained Dr Alving. Each is active against a number of the different HIV clades, and works by binding to either the gp41 or gp120 subunits formed from the gp160 polypeptide on the surface of HIV, thus preventing the virus from binding and entering host cells.

The most broadly neutralising of the antibodies identified are 2F5 and 4E10. These antibodies recognise practically all HIV clades and bind to both gp41 and phospholipids on the surface of HIV cells, and have become models for vaccine design, explained Dr Alving.

# Cell senescence may be useful cancer drug target

A better understanding of cellular senescence could yield new targets for cancer treatments, said Nicol Keith, professor of molecular oncology at the University of Glasgow.

Senescence, he explained, refers to the finite number of growth cycles that a normal cell is capable of undergoing. "Cancer cells keep on growing," he said. "They seem to overcome this natural barrier."

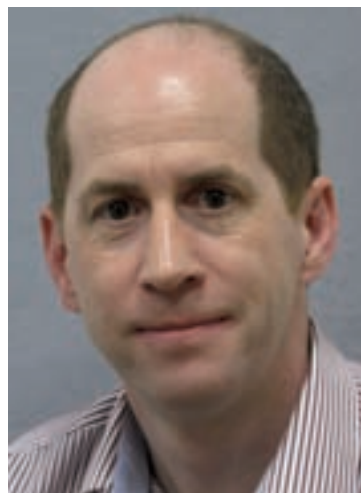
"Triggering senescence in cancer cells may be a useful strategy for anticancer drugs," he went on to suggest. Furthermore, he believes such research is warranted and timely, even though the process of cellular senescence is not fully understood. Nonetheless, he confirmed, it is known that cellular senescence can be induced by:

- Oncogenes
- Cellular stress
- Erosion of telomeres (DNA sequences at the end of chromosomes)
- Drugs

Of these four, the process that is best understood is telomere-induced senescence, said Professor Keith. It is believed that telomeres shorten over time and that senescence occurs

when they become too short. Professor Keith described research that has been conducted at the University of Glasgow to identify compounds that could inhibit the production of telomerase — an enzyme capable of slowing telomere erosion or, in certain circumstances, lengthening telomeres. "Inhibiting the expression of this gene will cause cell senescence," he explained.

Scientists at the university assessed "libraries" of compounds and identified several that repressed the gene that encodes telomerase. "Three of these were glycogen synthase kinase [GSK] inhibitors," he said. Further research went on to show that GSK inhibitors reduce cell growth and studies conducted on mice have shown that GSK inhibitors can delay tumour growth. "This gives us an animal model which we can use to



**Nicol Keith: need to better understand cellular senescence**

build up pharmacodynamic endpoints," he said.

The experiments did not induce full senescence, said Professor Keith, and this might be because most cellular processes can be performed using several different genetic pathways.

To circumvent this problem, research needs to identify which transcription factors act on the genetic pathways that are involved with cellular senescence. It might then be necessary to target more than one of these factors at the same time.

Translating this to the clinical situation will take many years, said Professor Keith. However, he noted that his team had not identified any toxicity issues so far with GSK inhibitors and he believes targeting cellular senescence, in general, is a promising approach for future anticancer treatment.

# NICE has approved 28pc of treatments

Nicola Cree reports on the aims and achievements of NICE and the development of companion diagnostic testing

The National Institute for Health and Clinical Excellence's budget has increased seven-fold in the past 10 years to £60m per year, chairman Sir Michael Rawlins told the conference.

This budget is expected to increase by £20–30m over the next three years, subject to what happens to public expenditure, he added.

The purpose of NICE is to supply health professionals with advice on attaining the highest standards of clinical care for NHS patients and to promote and sustain public health not only through the NHS but also to the wider public, said Sir Michael. To do this, two factors need to be taken into consideration — clinical and public health effectiveness and cost-effectiveness. NICE is required by law to take cost-effectiveness into account, he added. The cost of healthcare is getting more difficult, he said — monthly costs of cancer drugs have risen since 2007.

NICE guidelines have different statuses in different areas of the UK, Sir Michael explained. Technology appraisals are valid in England and Wales. They are mainly valid in Northern Ireland — where different legalities, such as abortion being illegal, have to be considered — and only partly cover Scotland.

Clinical guidelines cover England, Wales and Northern Ireland, interventional procedures cover all nations and public health guidance is confined to England. In England technology appraisals carry with them a “funding direction” — a legal requirement whereby NHS trusts are obliged to provide any NICE-approved treatment providing a clinician wishes to use it and a patient wishes to receive it, he explained.

NICE bases its guidance on five principles:

- Guidance is technically, clinically and scientifically robust

- Guidance is inclusive — so that everyone with an interest has chance to have a say
- The processes used and decisions made are transparent
- Advice is timely
- Guidance is independent — decisions are made by independent advisory bodies

Time-dependent advice is the one area where NICE has fallen down, Sir Michael admitted, mainly because ministers have to refer topics to NICE — this has, hopefully, been overcome, he added.

So far NICE has undertaken 180 appraisals — which may have included more than one decision — looking at 360 condition treatment plans. In about 28 per cent of cases, NICE has agreed to the use of treatments within the licensed indications, in over half of cases NICE has recommended restricted use and on a few occasions NICE has recommended treatments only for research — mainly for devices and procedures, not pharmaceuticals, Sir Michael said.

In about 10 per cent of cases, NICE has not recommended treatments and in five cases, manufacturers have declined to make a submission. This has mainly occurred recently, Sir Michael added, stating that it was probably because the company knew the treatment would not be affordable to the NHS — all of the drugs affected were anti-cancer treatments, he said.

There are always gaps in data on clinical and cost-effectiveness and members of advisory committees have to exercise judgement, he added.

As well as taking into account clinical effectiveness and cost-effectiveness, NICE has to balance efficiency and fairness, Sir Michael said. “We cannot spend £10m on one person's life. To do so would deprive many other people of life-saving forms of treatment,” he declared.



Nadia Attura

**Sir Michael Rawlins: release 2 of NHS Evidence to be launched in October**

Treatments costing below £20,000 per quality-adjusted life year (QALY) will be considered cost-effective; treatment costing above £30,000 per QALY will be considered cost-ineffective. However, there are some incidences when the appraisal committee will go higher.

Referring to the newly launched NHS Evidence, Sir Michael explained that it was designed to give healthcare professionals reliable information online. It is not currently perfect, he added but said that release 2 will be launched in October. “It will get better,” he told participants, and he asked health professionals to continue using it.

## Diagnostic testing should go hand-in-hand with drug development

Diagnostic testing should be combined with the development of pharmaceuticals, said Eddie Blair, managing director, Integrated Medicines.

Companion diagnostic testing can increase the return from a drug and can prevent the drop-off of profit after so many years — the pattern that usually occurs with pharmaceuticals, he said. Although there are some early costs with the development of diagnostics, it can give about a 10 per cent uplift in profit, he added. It is important to start the development of diagnostics at the end of phase I trials of the drug at the latest, Dr Blair added, since diagnostics can take up to 10 years to develop.

There are a number of key requirements of point-of-care diagnostics, said Ben Arlett, product development director, Atlas Genetics. It is essential that devices offer laboratory quality results in around 20 minutes — since it is believed that 20 minutes is the length of time a patient is willing to wait for a result. The system must be simple to use, he added, and capable of carrying out multiple tests on a single sample. The system must also have the ability to perform nucleic acid amplification tests and immunoassay, he said. In addition, it should be low cost and portable, he said. Point-of-care tests, other than pregnancy testing and glucose testing, have been slow to emerge because cur-

rent technology cannot deliver tests at an acceptable speed, cost and sensitivity, he said. Point-of-care diagnostic testing offers reduced costs while improving patient care, he added. However, benefits are generally only realised if action can be taken immediately (for example, quarantine or treatment). Point-of-care diagnostics can be used to test for sexually transmitted infections, screen for meticillin-resistant *Staphylococcus aureus*/*Clostridium difficile*/novovirus and to screen livestock at shows, races and auctions, he said.

Companion diagnostics are a stepping-stone towards personalised medicines, Dr Blair concluded.

# Developments in diabetes management

Diabetes is fast becoming a global epidemic — and the therapeutic options available are developing almost as rapidly. With diabetic patients often taking several drugs, medicines management is key to tackling the disease. **Francesca Rivers** and **Nicola Cree** report

Although early glycaemic control is important to reduce the risk of diabetes-associated complications, data suggest it is not achieved by most diabetic patients in the UK, said Michael Feher, consultant in diabetes and endocrinology at the Chelsea and Westminster Hospitals NHS Trust.

Most oral therapies for type II diabetes only address one aspect of beta-cell dysfunction with few focusing on islet dysfunction as a whole, observed Professor Feher. In addition to this, many of the existing treatments cause weight gain, hypoglycaemia and gastrointestinal side effects, and the durability of the glycaemic control achieved with any of the antidiabetes medicines declines over time.

Dr Feher also argued that the overall approach to treating diabetes represents poor practice. Using rising HbA<sub>1c</sub> levels as a marker for progressing a patient on from lifestyle advice to monotherapy and dual therapy, and finally to insulin and oral combination therapy, amounts to a “waiting for failure” approach, he said.

Anthony Barnett, professor of medicine at the University of Birmingham, agreed that current diabetes therapies have shortcomings, but highlighted incretin-based therapies as an exciting therapeutic development offering decided advantages over other drug classes in terms of their tolerability, weight neutrality and low hypoglycaemia risk.

“I believe there is a very significant place for these agents in diabetes management, which will get greater as time goes on,” he said, adding that a once weekly injection of liraglutide may appear on the market in the

next month. Bariatric surgery, such as gastric bypass surgery and gastric banding, is also gaining pace, and is a significant option for some types of patient, he added.

Dr Feher told the conference there is a strong pipeline for new diabetes medicines, with an explosion of novel drugs and targets, as well as new formulations of existing agents, seen over the past 20 years. But there remains a definite need to look for new treatments to tackle the global epidemic of the disease.

There are a number of physiological processes that new drugs could target, he argued, such as the glucose–fatty acid cycle, or the rate of gastric emptying or carbohydrate digestion and absorption.

Miriam Kidron, of Oramed Pharmaceuticals, told conference participants about work currently under way to develop a soft gel capsule for the oral administration of insulin. Clinical trials of the drug have shown promising results, with a reduction in the levels of glucose and C-peptide achieved, and an increase in plasma levels of insulin, she said.

“We submitted a package to the [US Food and Drug Administration] in July 2009, and we hope to get a response in October,” said Dr Kidron. She added that the technology is not particular to insulin, and could be applied to the oral administration of other peptides.

## Islet cell transplantation

Islet cell transplantation is being developed by Stephanie Amiel and a research group at King's College London as an option for the treatment of a subset of patients with type I diabetes.

Professor Amiel explained that few patients will be suitable for the procedure. It is not possible to introduce enough islets to overcome insulin resistance, so the treatment is not effective for the treatment of type II diabetes. For patients with type I diabetes, the period of immunosuppression required after transplantation makes it a high-risk treatment, and the procedure does not eliminate the need for insulin.

However, the transplantation — which involves administration of purified and concentrated islet cells directly into the portal vein via a drip, and brings about an improvement in glucose control — has proved a welcome new option for type I diabetic patients with severe hypoglycaemia that seriously affects their quality of life.

There are currently three islet cell isolation centres and six transplantation centres in the UK, and last year the programme was awarded NHS funding. Professor Amiel said the programme's current areas of focus includes improving immunosuppression and islet cell survival, and gaining better and more established sources of islets. At present, a single transplantation of islet cells requires the cells from two pancreases and ideally this would become a one-to-one donation. However, Professor Amiel is reluctant to abandon the multiple donor approach at this stage because of the high islet load required for successful transplantation.

## Glucose-sensitive hologram technology could remove need for finger prick blood glucose test

Patients could soon find themselves monitoring their blood glucose levels via a hologram placed in a contact lens, Chris Lowe, director of the institute of biotechnology, University of Cambridge, told participants at the conference.

Professor Lowe explained how his team is working on hologram research that would remove the need for patients to undertake a finger prick blood glucose test and allow them to measure their glucose levels in real time via a hologram placed in a contact lens.

The holograms, which are cheap, Professor Lowe said, will change colour based on a

chemical or biological signal, which changes the wavelength of visible light.

The glucose-sensitive hologram is based on a boronate system because boronate is one of the only substances that binds to glucose in an aqueous solution, said Professor Lowe. Before the contact lens technology becomes a reality, Professor Lowe's team has a few challenges to tackle, including the pH of tear fluid, which varies when eyes are closed, and sensitivity issues — because the tear level of glucose is about 0.3mM, whereas it is about 5mM in the blood.

There have also been issues with the physics of detection, Professor Lowe ex-

plained, because most holograms only read over about five degrees before their wavelength changes. However, the team now has a hologram that will read over 120 degrees with no changes. The envisaged contact lens would be changed daily by users, he said.

Currently, a glucose-sensitive hologram is undergoing in-dwelling catheter testing in humans.

Professor Lowe's team has created holograms as small as 10µg<sup>2</sup> and expect to be able to create them as small as 2µg<sup>2</sup>, he said. There will be an electronic output from the hologram system to send the results to GPs or hospital recording systems, he added.

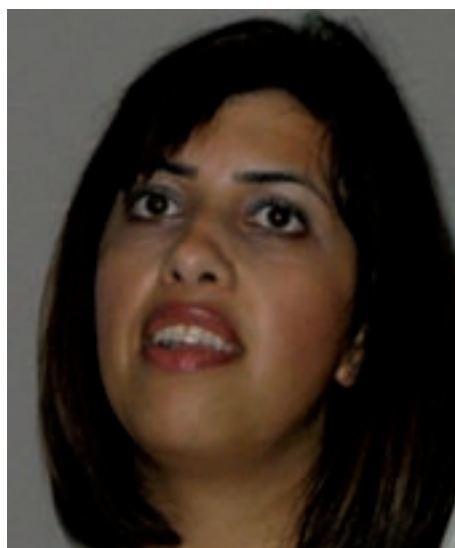
# Dismissing health inequalities in diabetes care

Cultural aspects affect the treatment of diabetes, Alia Gilani, health inequalities pharmacist, NHS Greater Glasgow and Clyde, told the conference.

The occurrence of diabetes is six times higher in those of South Asian origin than in white Europeans. In the area Miss Gilani works in Glasgow, there is a high number of such patients.

Within their culture many have a fatalistic attitude to the disease with a belief that their fate is in the hand of god, Miss Gilani explained. A lot of family life revolves around food and exercise is not common — with some believing prayer is a form of exercise, she added. There are concerns about the side effects of treatment and there is frequently a social stigma attached to the disease. It is also important to consider that patients may want to fast or take part in the haj, she said.

In addition to all the cultural considerations she has to consider when treating diabetes in patients of South Asian origin, Miss Gilani also explained how genetics can lead to a higher risk of long-term conditions. Although their body mass index is the same as that of patients of other origins, patients of South Asian origin have more centrally oriented fat distribution, which is a risk factor for cardiovascular disease. And although their total cholesterol measures are similar to those of indigenous populations, patients of South Asian origin have a lower high-density



**Alia Gilani: social stigma attached to diabetes in South Asian culture**

lipoprotein and a higher triglyceride level, she explained.

Many patients of South Asian origin also have problems accessing healthcare. To combat this problem Miss Gilani told participants how she works in the minority ethnic long-term medicines service (MELTS) — a service that invites patients to attend healthcare services conducted in their native language and operates outreach clinics in places such as

mosques, Sikh and Hindu elderly centres, volunteer groups and community pharmacies. Miss Gilani also works with other ethnic minorities as well as those of South Asian origin.

Patients can be referred into the service by others and she currently has 80 patients. With an average of two appointments per patient, Miss Gilani explained that her job entails undertaking a medication review and referring patients on to other services they may require, such as podiatry, exercise or social work. Miss Gilani said that she frequently texts patients to remind them to go to these appointments. In her clinic she is able to prescribe or change oral antiglycaemic agents, statins, antiplatelets and antihypertensives. The consultations have also led to the diagnosis of other conditions, such as cancer and thyroid disease, she added. She works closely with doctors, social workers and diabetes specialist nurses. The service also gets patients' families involved, since the culture is often family based, she said.

Citing an example of a 36-year-old African-Caribbean male, Miss Gilani told the conference how it took her 18 months — including three letters and six telephone calls — to get him into the service. The patient believed he was not diabetic because this is what he had been told by a doctor in Africa, she said. Miss Gilani explained that she managed to get him to have blood tests and start taking an oral antidiabetic drug to treat the disease.

## Tackling hypertension in patients with diabetes

Eighty per cent of diabetic patients die from cardiovascular problems, so it is important to remember that diabetes is a cardiovascular disease, said Candy Norris, consultant pharmacist — cardiovascular, Harrogate and District NHS Foundation Trust.

Blood pressure targets are the key, Miss Norris said, adding that in the past 10 years there has been a big change in blood pressure targets, which has given pharmacists the opportunity to participate in helping patients to meet these targets.

Many clinical trials have failed to meet blood pressure targets, with systolic blood pressure being the most difficult to control, she said. Diabetic hypertension is the most complex part of diabetes management, she added.

The key thing in treating hypertension is to get the blood pressure down and not to worry about which drug is used, she added. On average, in Miss Norris's Harrogate clinic, patients need three antihypertensive drugs — similar to results found in trials.

Pharmacists need to be directly managing the patients and helping with medicines management since these patients often take a large number of medicines, she said. Patients with diabetes also appear to have

more of a problem with drug intolerances, she added.

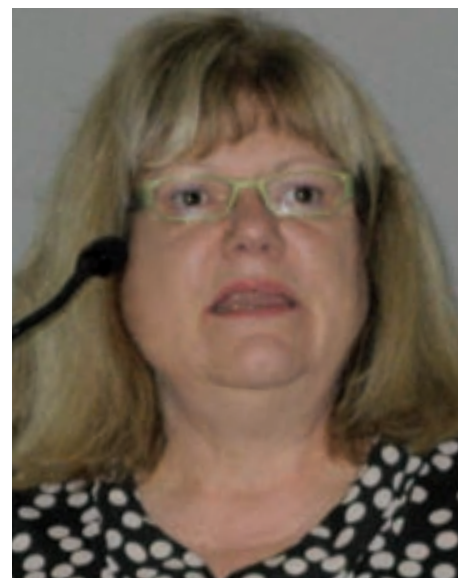
Miss Norris told participants about the secondary care clinic she runs, which focuses on cardiovascular risk and medicines management. Patients are seen for 20 minutes every four weeks and drug changes are initiated so that the patients can be discharged to their GP. A lot of these patients have medicines management problems that are discussed in a multidisciplinary team, Miss Norris said.

When dealing with patients on multiple drug treatments, it is important for pharmacists to build a relationship with each patient to help improve his or her confidence, she said. Miss Norris's clinic helps to enable patient to self-manage through hand-held records and a telephone helpline.

It is important that therapies are reinforced long term because there is evidence that blood pressure control starts to disappear in time, she added.

In the clinic, 68.3 per cent of patients referred achieved their blood pressure target on discharge. Feedback from GPs has also shown that they support the service and believe it is effective.

Eighty-eight per cent of patients felt very confident about a pharmacist looking after



**Candy Norris: building relationships is important**

their blood pressure tablets — the remaining 12 per cent were fairly confident.

In addition, 100 per cent of patients believed pharmacists listened to their concerns and provided reassurance.



Photographs by Craig Strong

Clockwise from top left: Fred Ayling, Pharmacists' Defence Association, demonstrates online services to Christine Lorenz, locum pharmacist, and Kay Seden, research and clinical trials pharmacist; Gul Root, principal pharmaceutical officer, Department of Health (left); Brian Curwin, chairman of the English Pharmacy Board, Royal Pharmaceutical Society; Gillian Hawksworth, former Society President, talks to conference participants; and Lesley Morgan, member of the shadow General Pharmaceutical Council with Steve Acres, technician member of the Society's Council



Photographs by Craig Strong

Clockwise from top left: Victoria Buyer, Protomed, and Elsabe Jones, pharmacist intern, Department of Health; Karen Hassell, professor of social pharmacy and school research director at the School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Christine Gray, shadow General Pharmaceutical Council staff, with Surider Kumar, prescribing support pharmacist; Sandra Melville, chairman of the Scottish Pharmacy Board, Royal Pharmaceutical Society; and Wendy Harris, the Society's deputy registrar and director of regulation

# Science abstracts — review 2009

A sample of the work reported in the science sessions at the British Pharmaceutical Conference is reviewed here by **Joseph Chamberlain**

Over 180 submitted science abstracts were presented at the British Pharmaceutical Conference. The highlights reported here were selected from the specialist podium sessions, with a short section on a personal choice from work presented as posters only.

## Pharmaceutical technology

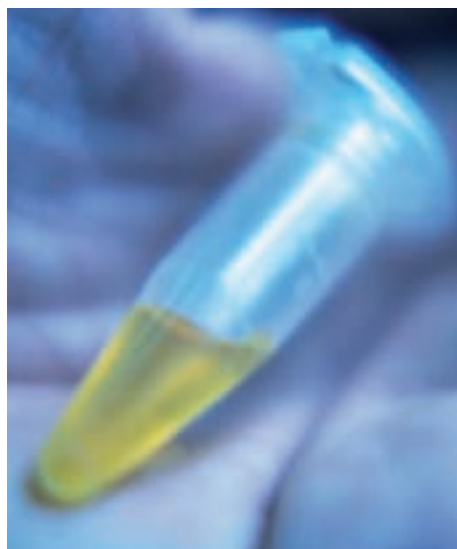
**Grant *et al*** (University of Liverpool) described how they overcame the problems associated with water-insoluble drugs. Organic nanoparticles were prepared *in situ* in a porous polymer by the technique of freeze-drying emulsions. The nanoparticles were slowly released from the polymer scaffold to form stable aqueous nanoparticle dispersions at neutral and basic pHs at room temperature. When the pH of the aqueous phase was reduced to 2, there was a much faster release of organic nanoparticles.

**Williams *et al*** (University of Nottingham) investigated some aspects of the effects of high-fat meals on the bioavailability of extended release formulations. Hydroxypropyl methylcellulose (HPMC) matrices rapidly formed gel-layer barriers and improved their extended release in milk and other emulsions containing up to 30 per cent fat. Drug release was progressively reduced with increasing media fat content. This work suggests that an environment containing emulsified fats is unlikely to promote accelerated drug release from HPMC matrices. A slowing of drug release is more likely, through an enhanced barrier at the gel-layer surface following fat deposition.

**Rauf *et al*** (Jamia Hamdard University, New Delhi) described a comparative evaluation of different techniques of taste-masking, including microencapsulation, ionic cross-linking, and drug-resin or ion-pair complexation. The products obtained for a water-soluble bitter drug, dicyclomine hydrochloride, were evaluated for taste masking and drug release. All the optimised products were tasteless and showed no drug release in buffer pH 6.8, the pH of saliva. For a sustained release of drug at physiological pH values, the microsphere-based formulations were the best.

## New scientists session

Baclofen is absorbed in the stomach or proximal part of the intestine and often shows low bioavailability. The development and evaluation of a novel floating *in situ* gelling system for stomach-specific drug delivery of baclofen was described by **Jivani *et al*** (Smt. R.B. Patel Mahila Pharmacy College, Atkot, India). Gelling systems were prepared by dissolving various concentrations of sodium alginate in deionised water, to which varying concentrations of drug and calcium bicarbonate were added. Gel was evaluated for *in*



Cristina Pedrazini/Science Photo Library

## Extract of the antimalarial drug cryptolepine: Ismail *et al* used microwave extraction methods to enhance yield and reduce impurities

*vitro* buoyancy and *in vitro* drug release. The prepared gel remained buoyant for 12 hours and released baclofen over the same period.

**Mercuri *et al*** (University of East Anglia) described the assessment of drug release and dissolution in the stomach by means of a dynamic gastric model (DGM), said to be a more bio-relevant approach than that using standard dissolution procedures. During fasted digestion, the release of nifedipine from two commercial formulations was different and consistent with *in vivo* data, supporting the claim that the DGM may provide a realistic temporal and dynamic model for the stomach environment.

## Medicinal chemistry

Metal ions, especially iron, mediate neurotoxicity in Alzheimer's disease, either by favouring beta-amyloid plaque formation or by redox cycling. **Roy *et al*** (King's College London) aimed to identify iron chelators able to cross the blood-brain barrier (BBB) and exhibit neuroprotective efficacy against oxidative stress in the brain. Several bidentate iron chelators (3-hydroxypyridin-4-ones) were synthesised based on the structure of deferiprone, a chelator used in the treatment of iron-overloaded thalassemia major. *In situ* brain perfusion was carried out on guinea-pigs using these chelators and deferiprone.

Chelators with a higher BBB influx efficiency than that of deferiprone were selected for neuronal cell culture studies to evaluate their neuroprotective efficacy against various oxidative insults. Four out of the 10 3-hydroxypyridin-4-ones fared better than deferiprone on the BBB influx index. Some chelators failed to cross the BBB. The molecular weight, lipophilicity, molecular volume and total polar surface area did not correlate with their BBB influx efficiency. Four 3-hydroxypyridin-4-ones with superior BBB influx efficiency to deferiprone were identified.

**Siddiqui *et al*** (Jamia Hamdard University, New Delhi) synthesised a series of new piperidyl indanone thioamides and assessed their anticonvulsant activity and neurotoxicity. All the compounds showed encouraging anticonvulsant activity and most were found to be less neurotoxic than the standard drug phenytoin. The most highly active compounds were subjected to further investigation by estimating the gamma-amino butyric acid (GABA) levels in the different regions of rat brain. It was suggested that the concentration of GABA increased significantly in the olfactory lobe and the mid-brain region of rat brain after administering some compounds. The thioamide derivatives of piperidyl indanone can be regarded as a newer class of anticonvulsant agents with potentially less neurotoxicity.

The ethanobotanical drug cryptolepine, used in malaria treatment and glycaemic control of diabetes mellitus, is usually obtained by time-consuming Soxhlet extraction of the dried roots of *Cryptolepis sanguinolenta*. **Ismail *et al*** (Liverpool John Moores University) sought procedures that diminished the risk of solvent ignition and toxicity by the use of microwave-induced extraction. A variety of polar solvents, especially ethanol in the presence of ammonia, proved highly efficient at extracting the crude alkaloidal material. Using microwaves ensured increased alkaloid extraction depending on the irradiation time. Trifluoroacetic acid proved superior to acetic acid as an extraction solvent. This method produced cryptolepine with less impurities associated with oxidation and dimerisation compared with conventional aerobic Soxhlet extraction.

## Materials science

During the process of micronisation to reduce the particle size of active pharmaceutical ingredients, a large amount of energy is applied to a material that can lead to changes in surface properties in an uncontrolled manner. **Parker *et al*** (Molecular Profiles, Nottingham) investigated the link between the mechanical properties, micronisation behaviour and surface energy of carbamazepine polymorphs using atomic force microscopy.

## BPC science abstracts 2009

The BPC science proceedings abstracts have been published as a supplement to *The Journal of Pharmacy and Pharmacology*. The abstracts can also be downloaded from [www.pharmpress/jpp](http://www.pharmpress/jpp).

Carbamazepine polymorphs could be ranked by Young's modulus and indentation hardness. Surface energy measurements showed an increase in surface energy after micronisation in all forms, which underwent a relaxation in surface energy following storage for four weeks.

**Meng *et al*** (University of East Anglia) explored the relationship between the composition and the associated thermal events of ethylcellulose films loaded with fractionated coconut oil, using modulated temperature differential scanning calorimetry and dynamic mechanical analysis to measure the glass transition temperature ( $T_g$ ) and detect potential phase separation processes. An endothermic event was observed around 180C, which was ascribed to melting of microcrystallites in the film. The  $T_g$  decreased when the coconut oil was added. However, on adding coconut oil beyond 20 per cent, the  $T_g$  remained constant at approximately 97C, while a lower temperature peak was observed at approximately 53C. Such phenomena have been associated with phase separation, so the presence of multiple mixed phases was indicated. The authors suggest the formation of binary mixed systems rather than pure component separation and proposed a novel method for estimating the associated composition.

**Garland *et al*** (Queen's University Belfast) described studies to aid in the optimisation of a formulation for use in controlled transdermal iontophoretic drug delivery by showing that the dielectric properties of poly(ethylene glycol) (PEG) crosslinked poly(methyl vinyl ether-co-maleic acid) hydrogels were dependent on polymer concentration, PEG molecular weight and swelling. The study was seen as evidence that these systems can be modified to serve as an electrically conducting matrix, which may suggest a method of altering the drug release profile of these films following the application of an electric field.

## Pharmaceutical science

**Cronin *et al*** (Liverpool John Moores University) assessed the potential of an *in silico* method to identify the skin sensitisation potential of active pharmaceutical ingredients. Such information was retrieved from publicly available safety datasheets supplied by pharmaceutical companies on their corporate internet sites. The analysis indicated that the coding of mechanistic chemistry is significantly associated with identifying the skin sensitisation potential of active pharmaceutical ingredients. Any misclassified compounds provided useful information to develop these rules further to handle issues such as metabolism and to extend the domain of the models. This provides a basis to extend the coverage of the rules for protein reactivity associated with skin sensitisation. Further, analysis of the structure of compounds that are identified *in silico* as having the potential for skin sensitisation, but for which there is no evidence, will provide information on structural mitigating factors such as deactivating groups. The

## Presentation of JPAG's Conference Analytical Science award



Isobel Cook (BioPharma Technology Ltd, Winchester, Hampshire) became the fourth recipient of the Joint Pharmaceutical Analysis Group's (JPAG) Conference Analytical Science Award at the British Pharmaceutical Conference this year.

The award is a certificate and a bursary of up to £2,000 for the recipient to attend a scientific meeting of his or her choice. It was awarded on the basis of the scientific quality, originality and potential impact of the work presented at the "Short papers in pharmaceutical analysis" session at BPC, in a paper entitled "A study of vial headspace moisture in an entire freeze-dried batch and the factors affecting moisture content variability".

The picture shows Ms Cook receiving her award from JPAG chairman Ray Munden.

results showed that useful toxicological information may be extracted from safety datasheets, which will assist in the development of *in silico* toxicological approaches.

Cyclodextrins can form inclusion complexes with terpenoids and, therefore, reduce toxicity, volatility and hydrolysis of precursors. They can also increase product yield through protection of formed products. **Abdelkader and Lockwood** (Manchester University) used beta-cyclodextrin to enhance biotransformation of terpenoids using plant cell cultures. Beta-cyclodextrin greatly extended concentrations of both substrate and product over extended periods at somewhat constant levels. Beta-cyclodextrin also enhanced biotransformation of terpenoids by decreasing availability of substrate in the suspensions, through inclusion complex formation, thus reducing its toxicity to plant cells and allowing for increased amounts of substrate to be fed without any harmful effect to the cells.

## Drug delivery

Disulphide-crosslinked polymers are redox-sensitive vectors that are stable in the extracellular medium but undergo dissociation in the reductive environment of the cell to facilitate plasmid release. Since crosslinking is believed to increase the molecular weight and size of the polymer, it has not been applied to high molecular weight polymers and there are always residual thiol groups on the polymer since not all thiols are crosslinked.

**Aravindan *et al*** (Reading School of Pharmacy) set out to investigate the nature of disulphide crosslinks, the role of thiols and the degree of crosslinking on transfection efficiency by comparing thiolated and crosslinked derivatives of polyethylenimine. Disulphide-crosslinking in crosslinked polymers is intramolecular and hence does not increase the molecular weight of the polymer. Therefore, disulphide crosslinking can be applied to relatively high molecular weight polymers without detrimental effects on cytotoxicity. Optimising the degree of crosslinking, and hence the concentration of residual thiol groups, can provide optimal polyplex stabilisation and increase cellular uptake, thereby increasing transfection efficiency.

**Rahmou and Elkordy** (University of Sunderland), noting that the formulation of stable and biologically active proteins is compromised by their chemical and physical instabilities, evaluated the crystallisation and spray-drying of lysozyme, a model protein, in the presence of different concentrations of two different surfactants (Caprol PGE860 and CremophorRH40) not previously used to stabilise proteins. Preparations were characterised using a bioassay and standard physicochemical methods. Storage stability studies were conducted for protein solutions for eight weeks at room temperature and above. The stability and biological activity of spray-dried lysozyme were found to be improved by the addition of surfactants. The best bio-

logical activity of lysozyme was observed with CaprolPGE860 in crystallised and spray-dried forms. The results show promise for preparation and delivery of stable and effective protein pharmaceuticals.

Vaginal rings are currently being developed by **McBride et al** (Queen's University, Belfast) for sustained delivery of single HIV microbicide compounds. The feasibility of providing simultaneous sustained release of maraviroc (an entry inhibitor) and dapivirine (a non-nucleoside reverse transcriptase inhibitor) from matrix-type vaginal rings was evaluated. The study demonstrated for the first time that microbicide combinations may be effectively incorporated within a single matrix-type vaginal ring device to provide sustained release of HIV microbicides at rates independently determined by their initial loading. Such combination vaginal rings may ultimately be useful in providing broad protection against sexually transmitted HIV infection.

### Pharmaceutical analysis

Freeze drying (lyophilisation) is used for production of pharmaceuticals, vaccines, diagnostics and other materials to prevent loss of activity and increase product shelf life. To demonstrate uniformity of the process **Cook et al** (Biopharma Technology, Winchester) developed a method of determining residual water content throughout a batch. Vial headspace moisture was mapped using frequency modulated spectroscopy (FMS) after different lyophilisation cycles in a laboratory freeze dryer. FMS is a high-sensitivity laser absorption technique and can be used to measure partial pressure of water within the headspace of each vial. For sucrose and mannitol excipients, the effect of varying product and process parameters on headspace moisture could be assessed and these values correlated with total residual moisture as measured by the conventional Karl Fischer method. Thus, FMS may enable complete batch inspection due to the speed of the analysis and its non-destructive nature and has the potential to be fitted into a quality-assurance framework. For this presentation Isobel Cook was awarded the Conference Analytical Science Award, sponsored by the Joint Pharmaceutical Analysis Group (see Panel, p28).

The chemical shifts of different non-exchangeable aromatic protons of mebeverine hydrochloride migrate to different extents as the concentration of the analyte is varied in aqueous solution. This concentration-dependent chemical-shift variation is linear across a useful range, and it has, therefore, been applied by **Elmasrya et al** (University of Bath) to the quantitative analysis of mebeverine HCl in its pure form and in pharmaceutical tablets. Comparison of the nuclear magnetic resonance (NMR) spectra obtained at different concentrations showed that the chemical shift of the mebeverine HCl aromatic protons changed with changing concentration in D<sub>2</sub>O solution; a quantitative NMR assay of mebeverine HCl in



**Apples grown organically contain more healthy components, according to research by Li and Wakeman**

D<sub>2</sub>O was thus developed showing acceptable characteristics regarding accuracy, precision and robustness.

An increased level of discomfort has been reported from specific batches of some injectable hyaluronic acid products, and it has been proposed that this may be due to the presence of traces of bacterial M protein fragments, membrane proteins remaining after hyaluronic acid purification. **Taylor and Rae** (Reading Scientific Services) reported on the development of an analytical method to identify and confirm the presence of M protein fragments in hyaluronic acid preparations. Proteomic fragments were identified by the enzymatic digestion of hyaluronic acid solutions using trypsin protease, and liquid chromatography-mass spectrometry analysis was carried out to compare the digested and undigested samples. The M protein fragments were detected in samples of hyaluronic acid preparations where an inflammatory response had been previously reported, and subsequent analysis of samples where no inflammatory response was reported yielded no detectable M protein fragments. This work supports the hypothesis of streptococcal M protein contamination of hyaluronic acid preparations being responsible for the inflammatory response reported.

**Assi et al** (The School of Pharmacy, London) demonstrated the identification of tablets still contained in their blister packaging by near-infrared spectroscopy. Twenty-seven batches of various products in colourless transparent blister packaging were purchased from the world market. Ciproxin, which was available in multiple batches, was used to standardise the system. The spectra of the tablets were produced with a FOSS 6500 near infrared (NIR) spectrometer using a Smart Probe and processed as standard normal variate second-derivative spectra. Comparison of the spectrum of a standard Ciproxin tablet with a variety of other tablets in their blisters was made using correlation in wavelength space and principal component analysis to provide a numerical and graphical

profile of the tablets. Of the 20 products, only three mismatches were observed, which may be due to the similar composition of excipients in the particular products. The precise position of the probe in relation to the blister and the tablet was investigated and found to have little effect. However, NIRS could not be applied to coloured, opaque or aluminium foil-packaged tablets.

### Posters

**Dearden et al** (Liverpool John Moores University) proposed a new quantitative structure-activity relationship (QSAR) model for human skin using readily available molecular descriptors. The high cross-validated correlation coefficient indicates that the QSAR can reliably be used for predictive purposes. Several other authors proposed computer routines for predicting toxicity or carcinogenicity of drug molecules, including toxicity modelling of benzodiazepine drugs by partial least square analysis by **Suzuki and Funar-Timofei** (Toyo University, Tokyo), carcinogenicity modelling of diverse chemicals based on substructure grouping and support vector machines by **Tanabe et al** (University of Tsukuba, Japan) and prediction of environmental toxicity of pharmaceuticals by **Madden et al** (Liverpool John Moores University).

**Teow et al** (University of Central Lancashire) described the use of a dendrimer carrier to enhance paclitaxel delivery and bypass the P-glycoprotein efflux transporter. Enhanced permeation of paclitaxel across the monolayers of Caco-2 cell was found when conjugated to surface-modified G3 dendrimer.

**Patel et al** (De Montfort University, Leicester) described the development of a dried blood spot (heelstick), and thus the microvolume sampling methodology, for dexamethasone to facilitate pharmacokinetic studies in paediatrics.

**Zughaid et al** (King's College London) investigated the age-old problem of improving the absorption of hormones cortisol and progesterone by studying their solubilisation by simulated intestinal fluids containing lipids. Incorporation of lipid digestion products in the formulation increases the solubility of these lipophilic drugs and such complex media may provide more relevant fluids for dissolution and permeability screening.

**Li and Wakeman** (Eden Healthcare Technologies, Leicester) used high-performance liquid chromatography to characterise eight beneficial secondary plant metabolites in the flesh and peel of 15 varieties of apple. There were significant differences in the levels of beneficial phytoalexins between different varieties of apples and apples grown organically and apples grown non-organically. Organic apples consistently contained higher levels of all analysed components, and more healthy components were concentrated in the peel. A 12th century apple, Pendragon, contained the highest levels of all components.

Brad Collins/Dreamstime.com