Midland Hospitals Opening November

Summer 2015

— An HPS publication —

Newsline

Clinical contribution by HPS Pharmacies

St John of God Partners with HPS

at Midland Public and Private Hospitals, and HPS' Innovative ClinPod® 2015 Upgrade Facilitates Optimised Mobile Patient Care

Plus:

HPS' Annual Gala and Awards Evening

HPS Pharmacies

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HPS works to enable the delivery of premium pharmacy services to hospitals and other institutions, by its network of approved pharmacies. HPS Pharmacies are approved and regulated pharmacy businesses, operating under the HPS banner.

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This Knowledge Centre contains an array of clinical articles prepared by HPS Pharmacies, which are approved and regulated pharmacy businesses.

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HPS has a particularly strong period of growth approaching...

Message from Tony Wyatt

As we look towards the exciting year ahead, HPS and its network of pharmacies celebrates the close of another highly successful year for the business in 2014. In line with HPS' strategic plan for growth, it was pleasing to see HPS' footprint in both New South Wales and Victoria further expanding with the opening of two new HPS sites at Waratah Private Hospital and The Melbourne Clinic. As HPS' site presence expanded, so too did the business' renewed focus on compounding. In 2014, a further investment in compounding resources, including equipment and specialist staff, allowed HPS to deliver an even greater scope of services to our valued clients.

The momentum gathered from last year's developments has provided a strong platform for HPS to commence 2015. To continue this momentum, HPS' Executive team recently convened to solidify and endorse HPS' strategic plan for the upcoming twelve months and beyond.

I am pleased to announce that the new St John of God Midland Public and St John of God Midland Private Hospital development in Western Australia is due to open in November, after three years of construction. HPS were successful in securing a contract with St John of God for the provision of pharmacy services at the extensive development in 2011 and I am very excited that HPS will be on-site at the hospital in November 2015. This valuable partnership presents an exciting opportunity for HPS to further expand its public hospital footprint and HPS' presence in Western Australia. HPS has a longstanding partnership with St John of God Health Care and we are delighted for the opportunity to add further value through an extension of our services to

the St John of God Midland Public and St John of God Midland Private Hospital. To read more, please turn to page 6.

HPS' IT department have delivered exceptional results in the upgrade of the business' innovative proprietary software, ClinPod® 2015. I am excited by the numerous benefits that ClinPod® 2015 provides to our valued clients as we continue to invest in developing state-of-the-art IT solutions to facilitate the growth and evolution of pharmacy care. ClinPod® 2015 represents a great leap in pharmacy innovation, and I applaud all involved for their commitment to excellence and outstanding developments with the application. To read more, please turn to page 8.

The iconic Adelaide Oval provided an ideal venue to celebrate HPS and its network of pharmacies' successes over the past twelve months and recognise key performers within the business. The event concluded HPS' annual Management Group Conference (MGC) at which leadership and fostering teamwork was of particular focus. This conference proved productive and innovative once again, cementing its place on the HPS calendar as a valuable platform for collaboration, with in-depth discussions assisting to develop strategies for the year ahead. To read more, please turn to page 10.

In recognition of HPS Pharmacies' commitment to quality, I am pleased to communicate HPS has received several exciting industry accolades in the past quarter.

Recently, HPS – Warrnambool was awarded the highest merit score for the *Australian Council on Healthcare Standards'* (ACHS) *Governance and Systems for Medication Safety* accreditation criteria. I would like to congratulate HPS – Warrnambool Pharmacy Manager, Kate Bailey, and her team on this wonderful achievement and demonstration of excellence.

> This valuable partnership presents an exciting opportunity for HPS to further expand its public hospital footprint...

Additionally, HPS were finalists in two awards for its internal eLearning induction program. HPS were recognised in the *Best Induction* category at the *LearnX Impact Awards 2014,* and in the category of *eLearning Achievement* at *The Australian Institute of Training and Development's* (AITD) *2014 National Training Excellence Awards*. These accolades reflect the investment and importance HPS places on eLearning to facilitate employee development within an ever changing regulatory landscape.

Operationally, HPS has a particularly strong period of growth approaching in Victoria, with two new on-site pharmacies and two refurbishments in progress. The two new on-site pharmacies in Victoria are important extensions of existing partnerships, and support HPS' charter for growth. Additionally, the site refurbishments will ensure all HPS sites remain on the forefront of quality and safety, which is in line with HPS' robust Quality Improvement & Compliance initiative launched in 2014. To read more, please turn to page 12.

Furthermore, HPS is dedicated to delivering the highest quality services to its existing valued clients, and always strives to ensure we are meeting their dynamic needs. As such, I would like to take this opportunity to thank our current clients who participated in HPS' 2014 Client Surveys. These annual surveys are an important tool for HPS to gain valuable feedback and insights, allowing us to refine our operations to ensure we continue to evolve with our client's needs. In line with HPS' commitment to Corporate Social Responsibility, we will be donating in excess of $2,000.00 to charities on behalf of our clients, whom raised $10.00 for every survey completed.

I am inspired by what the year ahead will bring to HPS and our valued clients. HPS' success in 2014 has continued to take HPS from strength to strength, and has further solidified the business' position as Australia's leading service provider. I look forward to sharing with you future developments throughout the year.

Tony Wyatt
Partner/Chief Executive Officer

Cover page: Artist impression of St John of God Midland Public Hospital.
This page: (top) Artist impressions of St John of God Midland Private Hospital entrance, and (bottom) St John of God Midland Public Hospital Emergency entrance.

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St John of God Partners with HPS for Public and Private Hospital Development in Midland

HPS are excited to announce an extension of its valuable partnership with St John of God Health Care at a new development in Western Australia. St John of God Midland Public and St John of God Midland Private Hospital are currently undergoing construction, with an expected opening date of November 2015. The hospitals, a public private partnership with the Western Australian State Government, will be collocated within one complex, with 307 public beds and 60 private beds, 80% of which will be single occupancy. This represents a larger and more comprehensive health care facility closer to home for the local community.

> *"Working with HPS will complement our commitment to excellence in all aspects of patient care due to their depth of experience..."*
>
> – Dr Glen Power, Chief Executive Officer, St John of God Midland Public and Private Hospitals

"Working with HPS will complement our commitment to excellence in all aspects of patient care due to their depth of experience in providing hospital pharmacy services. They will play an important role in the provision of a holistic service for inpatients and outpatients", says Dr Glen Power, St John of God Midland Public and Private Hospitals Chief Executive Officer.

"HPS Pharmacies are delighted to be providing on-site pharmacy services to both the public and private hospitals. Having worked with St John of God Health Care for several years at St John of God Warrnambool Hospital, we look forward to further strengthening this successful partnership. Furthermore, HPS look forward to extending this partnership to the public sector, and anticipate a highly successful delivery of patient care across the entire campus", says Tony Wyatt, HPS Partner and Chief Executive Officer.

St John of God Health Care have established a national reputation for consistently providing excellent, compassionate care to a range of communities, and in conjunction with HPS Pharmacies, will continue to provide this high quality care to the communities of Midland and surrounding areas.

Tin Huynh, Partner and General Manager – Business Development at HPS says, "This represents an enormous opportunity for HPS to partner with a leading hospital provider to deliver pharmacy services to public and private patients in the Midland area. HPS is extremely excited to be involved and looks forward to playing a key role in the delivery of health services".

HPS' second on-site pharmacy in Western Australia will deliver a responsive and quality dispensing and oncology pharmacy service. The state-of-the-art facility will allow for the provision of the highest quality of patient care via an all-encompassing pharmacy service. As a core value of HPS, innovation is deeply ingrained into HPS' vision for health care.

St John of God Health Care together with HPS Pharmacies will incorporate a high level of technical innovation. Patient and medication data will be seamlessly and automatically exchanged between HPS' ScripTrack® and ClinPod® 2015 applications, and the hospital administration and clinical management systems. This level of data integration will greatly assist in the efficient patient flow through the hospital resulting in minimised waiting times, particularly at discharge time.

"Transparent, automated transmission of patient and medication data facilitates improved patient outcomes with reduced risk, improve upon efficiencies and enhance hospital accreditation criteria. Particularly in the public hospital, the data extends out into the public health systems and forms an integral part of the electronic discharge summary which ensures information is available to other health providers in a timely manner" says Ian Bell, HPS' Chief Information Officer. HPS will also be installing advanced high-speed robotic dispensing machines to further maximise efficiencies and to provide rapid, automated dispensing of the majority for patient medications.

Dr Power shares HPS' vision for an innovation driven, highly effective health care facility. "We are aiming to provide the best possible patient experience at the new hospital, using evidence-based care supported by the latest technology and by partnering with innovative providers, such as HPS".


SMITH, RUTH
Details Review Medications Interventions
ClinPod

HPS Facilitates Mobile Clinical Care with ClinPod® 2015 Upgrade

HPS' proprietary ClinPod® application, already recognised as one of the industry's leading clinical pharmacy applications in Australia, has recently undergone an exciting major upgrade and is now conveniently delivered on mobile tablets to facilitate real-time bedside delivery of pharmaceutical care and superior patient outcomes.

"The upgraded ClinPod® 2015 is an immense step forward for clinical pharmacists and represents the transition from paper based systems of medication management and clinical intervention, to portable, electronic resources. It is an easy to use, intuitive tool and is among the first of its kind. I'm very pleased to have been involved in the pilot phase and look forward to seeing the evolution of this ground breaking software", says Dina Dinh, Clinical Pharmacist at HPS – Melbourne Private.

> ***"Innovations such as ClinPod® 2015 have the ability to change the landscape of bedside care..."***
>
> – Alan Tuxford, Regional Operations Manager – VIC/TAS, HPS

The valuable mobility introduced to ClinPod® 2015 allows HPS Pharmacies' clinical pharmacists to easily coordinate, document and evaluate clinical activities, including the ability to prepare full Medication Management Plans at the patient bedside. ClinPod® 2015 increases the efficiency of pharmacists' time and enhances the timely resolution of medication therapy related issues and seamlessly refers matters to other health practitioners for action.

Ian Bell, HPS' Chief Information Officer, says "ClinPod® 2015 can harmoniously integrate the actions of clinical pharmacists into the functionality of the hospital. The application enables timely communication of medication related patient issues, medication interventions and facilitates effective communication channels between staff, patients, pharmacy, doctors and the admitting doctor". The upgraded software has the ability to send electronic medication discharge summaries directly to a patient's General Practitioner, alleviating the need for manual follow-up or patient recall. This smooth, automated and real-time reporting facilitates the continuum of care via the flow of accurate medication management information back into the community and also allows for a greatly improved and reliable source of medication history information should the patient be readmitted.

ClinPod® 2015 has been pro-actively developed to integrate SHPA (*The Society of Hospital Pharmacists of Australia*) standards of practice for clinical pharmacy services and is fully compliant with the *Pharmaceutical Society of Australia's* guidelines for pharmacists performing clinical interventions (D.O.C.U.M.E.N.T). Building clinical practice standardisation into ClinPod® 2015 will facilitate the delivery of care that improves patient outcomes, quality and safety.

Clients will have access to comprehensive reports relating to the pharmaceutical care activities provided by clinical pharmacists. These reports can be generated via a web portal, creating total service oversight and transparency. HPS' ClinPod® 2015 provides a complete audit trail of interventions and manages handover notes entirely automatically, not only providing essential patient specific medication management information for nursing staff but also saving valuable time. Patient medications may be fully monitored from pre-admission, throughout the admission stay, and finally onto discharge with any adjustments clearly identified to enable complete medication reconciliation and accurate sharing of information.

A comprehensive and fully documented delivery of pharmaceutical care improves the overall risk management of medication related matters for hospitals. "An added function of ClinPod® 2015 is the ability to document and report the severity scores for all medication interventions. This enhanced method of event reporting will improve the quality of communication between both staff and hospital administration allowing for the potential to develop improved medication management systems that minimise risk. Importantly, ClinPod® 2015 will assist hospitals to achieve medication safety goals related to meeting accreditation standards", says Alan Tuxford, HPS' Regional Operations Manager – VIC/TAS.

Improvements in information quality and communication has the potential to decrease hospital readmissions due to adverse medication events. "Innovations such as ClinPod® 2015 have the ability to change the landscape of bedside care for HPS and we are very proud to begin introducing this solution to our clients and to our pharmacists. The initial pilot stages have revealed very positive outcomes for patient care, with increased efficiencies and enhanced reporting", says Alan.

Tony Wyatt, HPS Partner and Chief Executive Officer says "I would like to congratulate HPS' IT department who have once again delivered upon the business' core value of innovation, developing a robust solution for our valued clients, patients and employees that facilitates an optimised delivery of pharmaceutical care".

This page: Entertainers and attendees of HPS' Annual Gala and Awards Evening 2014.
Bottom left: Award winners (from left); Niki Singh, Pharmacist In-Charge at HPS – Melbourne Private, Kristen Peck, Pharmacy Technician at HPS – Riverina, Rhona Selkirk, Clinical Pharmacist at HPS – Toowoomba, Rania Najjar, Pharmacy Manager at HPS – Modbury and Angie Lawson, Systems Training Manager at HPS – Corporate Office.

A Taste of Morocco at Adelaide Oval for HPS' Annual Gala and Awards Evening

HPS celebrated the successes of 2014 at the illustrious Annual Gala and Awards Evening in November. Over 170 HPS employees and their partners attended the iconic Adelaide Oval overlooking spectacular views of the Adelaide skyline.

This state-of-the-art venue provided a stunning backdrop for the Moroccan themed feast while guests were entertained by captivating dancers, palm readers and snake charmers. The earthy scent of incense, flickering tealight candles and the sounds of traditional music amalgamated to delight the senses and transport guests to a faraway land.

As fire twirlers lit up the sky, the event lent seamlessly to a mood of celebration as attendees reflected on the significant contribution from HPS' national teams. Now in their fourth year, the awards are celebrated throughout the business as a remarkable accolade and an honour to receive. The national awards encapsulate HPS' core values of excellence, innovation, leadership, respect and accountability, and acknowledges those employees and teams who excel in demonstrating these values throughout the year.

The six awards introduced and presented by HPS' Partner and Chief Executive Officer, Tony Wyatt, and Chairman of the HPS Board, Dr. Andrew Holsman, include:

"The Dr. Holsman award for Innovation", recognising outstanding innovation at any level of the organisation;

"Corporate Team Member of the Year", recognising that individual whose conduct and contribution had a profound impact upon the business and its employees;

"National Pharmacy Manager of the Year", recognising the outstanding leadership of a Pharmacy Manager within a team environment;

"National Site of the Year", recognising the leading HPS Pharmacies site for financial and team performance;

"National Pharmacist of the Year", recognising the company's most outstanding pharmacy professional for contributions to HPS, it clients, and the field of pharmacy within healthcare; and

"National Pharmacy Technician or Courier of the Year", recognising that individual whose conduct and contribution had a profound impact upon the business and its clients.

On the evening, Tony said "HPS is deeply committed to excellence across all aspects of the business, and these awards are a unique opportunity to recognise the individuals that have demonstrated their embracement of HPS' core values.

"I would like to thank the entire national team for their outstanding contribution and sincerely congratulate those who have achieved individual recognition through these HPS annual national awards".

The Annual Gala and Awards Evening was the conclusion to another fruitful Management Group Conference (MGC). Also held at the Adelaide Oval, the exclusive conference provided a unique opportunity for pharmacy and corporate managers nationwide to congregate for an information-dense and interactive three day conference.

"The environment created by the management team's participation and enthusiasm for discussion brought forward a strong, united vision for the business' endeavours in 2015. I look forward to the initiatives that have been formed as a result of the conference to further deliver the highest quality of pharmacy services to clients and patients", said Tony.

National Award Winners

Congratulations to our award winners who have been immortalised on the HPS Honour Boards at HPS' Corporate Office:

1. **The Dr. Holsman Award for Innovation**
   Rania Najjar
   (HPS – Modbury, South Australia)

2. **Corporate Team Member of the Year**
   Angie Lawson
   (HPS – Corporate Office, South Australia)

3. **National Pharmacy Manager of the Year**
   Niki Singh
   (HPS – Melbourne Private, Victoria)

4. **National Site of the Year**
   HPS – Modbury
   (South Australia)

5. **National Pharmacist of the Year**
   Rhona Selkirk
   (HPS – Toowoomba, Queensland)

6. **National Pharmacy Technician or Courier of the Year**
   Kristen Peck
   (HPS – Riverina, New South Wales)

From The Team

Rania Najjar

Site Manager, HPS – Modbury

Modbury Hospital is the largest public hospital in South Australia serviced by HPS Pharmacies, with HPS providing the highest quality pharmacy services for over 20 years. In collaboration with SA Pharmacy, HPS Pharmacies has delivered patients with greater access to medications and pharmacist advice by introducing significant pharmaceutical reforms by way of the *Pharmaceutical Benefits Scheme* (PBS). The *PBS* offers affordable, dependable and timely access to essential medicines for Australians, ensuring optimal health outcomes and economic benefits are achieved.

At HPS' Annual Gala and Awards Evening in November, I was honoured to receive the *Dr. Holsman Award for Innovation* for the successful implementation of these reforms at HPS – Modbury. The commission from SA Pharmacy for Modbury Hospital resulted in significant changes in the form of an expanded pharmacy team, enhanced work flows, additional clinical services and a newly refurbished pharmacy location. The successful implementation of *PBS* reforms has resulted in further optimised care for patients and the local community.

Additionally, I was proud to accept the *National Site of the Year* award on behalf of the entire team at HPS – Modbury. Over the period in which the reforms were implemented, the staff at HPS – Modbury flourished. HPS – Modbury were awarded the honour for continuing to deliver the highest quality pharmacy services to Modbury Hospital during the transition.

Alan Tuxford

Regional Operations Manager – VIC/TAS

2015 brings with it many exciting developments and significant investment by HPS into its Victorian sites. Two new on-site pharmacies at The Melbourne Clinic and at The Victorian Rehabilitation Centre, a refurbishment at HPS – Ringwood, and relocation of HPS – John Fawkner within the upgraded hospital represent HPS' commitment to continuous improvement and confidence that HPS' clients have in the business.

HPS has a long standing relationship with Healthscope, one which continues to strengthen and grow with the opening of these two new on-site pharmacies. HPS has serviced both The Melbourne Clinic and The Victorian Rehabilitation Centre for many years, providing high quality services from an off-site location. HPS have been invited to continue this service on-site, delivering additional client and patient benefits that come from an on-site pharmacy model, including rapid response times and immediate access to HPS Pharmacies' pharmacists.

Additionally, and in line with HPS' commitment to continuous quality improvement, I am pleased to announce that HPS – Ringwood has undergone an exciting refurbishment. This investment by HPS includes a dedicated room with filtered air supply for the isolator, and air filter extraction. Furthermore, HPS are preparing for relocation within John Fawkner Private Hospital. This relocation and investment in a new pharmacy provides HPS Pharmacies with an opportunity to cater for the expansion and upgrade of John Fawkner Private Hospital and will also include a refurbishment of HPS' existing oncology suite to further enhance patient care.

Angie Talbot

Compounding Sales Manager – Veterinary Services

As HPS continues to strengthen its investment in compounding, I have recently been appointed to a newly created role as Compounding Sales Manager – Veterinary Services. My role encompasses liaising with veterinary clinics in order to further grow and strengthen these key client relationships, providing product advice and maintaining an effective and efficient communication channel. As part of this role, I am responsible for developing long-term partnerships with veterinarians and nurses, working with new and existing clients to identify the issues that are most commonly faced when finding suitable and effective medications to treat patients.

HPS Pharmacies has over 35 years' compounding experience, including high quality veterinary compounding and have a dedicated specialist compounding team located at HPS – Alexander Avenue, in South Australia. This team works closely with myself and HPS' valued clients to ensure the best possible medication solutions are delivered to each individual patient, unique to that patient's particular needs.

HPS' investment in a dedicated veterinary compounding resource provides practices with a contact that is committed to the optimisation of patient care. I am looking forward to the advancements in compounding that HPS can achieve with this renewed focus and investment toward the industry.

Janene Garde

Partner/Clinical Publicist

This year has marked the 30th anniversary of both my commencement with HPS Pharmacies and the launch of Newsline. One of my earliest tasks at HPS was the creation of this publication. At its inception, Newsline began as a two page typed and photocopied bulletin that was distributed to our clients with the ward deliveries. Little did I imagine that I would have the pleasure to still be part of HPS, let alone Newsline, three decades later. Newsline has developed from a spare-time project completed in the short time between dispensing and clinical duties; to the publication as we know it today, where it has become a high quality product that demands the contributions of HPS' 170 knowledgeable pharmacists, my own formalised peer review and editorial skills, and the expertise of the entire Marketing department to design, proof and publish. In fact, the evolution of the quality to be found in Newsline could be an allegory to describe the development of the whole health care industry.

As with Newsline, the ability of HPS to develop innovative solutions for clients has continued to expand over HPS' forty years of operation. It has been an incredible journey to witness the transformation of pharmacy from when I first began with HPS Pharmacies, to the technologically driven industry it is today. Guided by an approach that solutions are always to be found, given proper enquiry and the diligent application of the right skills, HPS now has the technology, resources and capabilities to deliver services and products that were distant dreams thirty years ago.

Pharmacy Business

Australian Pharmacists at World War I

April 25th 2015 marks the 100th anniversary of the ANZAC landings at Gallipoli. HPS and its network of pharmacies would like to commemorate the role of pharmacists in World War I (WWI) and has invited guest author, Mia Bell, to provide an account of her family's involvement.

Not all of the servicemen who went away to the First World War were fresh-faced young men of 19 and 20 years of age.

My great grandfather Percival Dudley Belcher, known to his family as "P.D.", was at the time of enlistment in March 1917 some 37 years old with a wife and young daughter, and owned a pharmacy in North Sydney. His occupation was listed as "Registered Chemist" and his rank was Staff Sergeant Dispenser in the Australian Army Medical Corp.

Records from the Nominal Roll held by the Australian War Memorial list 147 Australian Staff Sergeant Dispensers, otherwise known as Pharmacists or Registered Chemists, serving in their professions as part of the war effort overseas.

The role of pharmacists in WWI is little documented, but was undoubtedly a valuable contribution and greatly assisted the rapid medical advancement of this time.

The Nominal Roll of Staff Sergeant Dispensers lists all of the Australian pharmacists who served in the Great War, beginning with the first pharmacist Edmund Bull, age 22, from Cheltenham NSW, who embarked on the *HMAT Ballarat* on 16th February 1916. All 147 pharmacists are listed, right through to Alwin Curwood, who at age 26 from Grafton NSW, was the last of the Australian Staff Sergeant Dispensers, and embarked on the *SS Carpentaria* on 7th November 1918, just prior to armistice and was subsequently recalled. The ages of the pharmacists in the unit of Staff Sergeant Dispensers range from 22 to 50, variously listed as Chemists or Registered Chemists (with one Labourers Chemist). Each record includes the chemist's marital status, religion, next of kin, and the ship on which they departed for war. All were paid at a daily rate of 11 shillings. From this we build a picture of professional men, many married, sailing off to war at a rate of one pharmacist on each ship; until we come to *HMAT Persic*, which accommodated only medical personnel, and included 30 pharmacists.

Dispensaries sat within field hospitals dispensing what we would now consider basic medical treatments (in a world pre-antibiotics) however fulfilling a vital role in the treatment of wounded soldiers. Common injuries were bullet wounds, gassing, shell shock, and epidemics of cholera. The military hospitals in India were less likely to receive wounded from the battle front but rather dealt with virulent outbreaks of malaria, heat exhaustion, dysentery, lice and venereal disease as well as mental illness caused by combat. Chemists were also responsible for securing water sanitation.

In the years from 1916 to 1918, roughly one third of all deaths in the Australian Light Horse Brigade were due to disease rather than battle casualties. Primitive sanitation and a poor diet contributed to a constant battle against cholera, dysentery and lice, but the greatest challenge came from malaria and influenza. Malaria often led to a secondary infection which would be the actual cause of death. Troop numbers were so depleted by malaria and influenza that treatment and prevention became a real focus. The large number of malarial cases led to the development of a malarial prevention plan consisting of a mobile unit travelling behind the Light Horse Brigade mounted troops, to facilitate prevention measures, and quickly diagnose and treat malarial fever. The main treatment was quinine, which was considered too unpalatable to the troops to administer in a preventative dose.

There was a similar interest in the diagnosis for influenza, for which the treatment was mainly nursing care and hospital rest. The influenza epidemic greatly affected medical personnel who came into constant contact with the disease. The symptoms of malaria and influenza often presented in a similar way, and so medical research focused on the identification and diagnosis of the two illnesses. The vital importance of having healthy troops ready for active service drove this focus on accurate diagnosis, disease prevention and effective treatment.

The services of the pharmacists who served Australia in WWI were integral not only to the health of the Australian Troops, but also to the advancements that have progressed pharmacy and health care to where it is today.

Percival Dudley Belcher (1880 – 1955)

Born in 1880 in rural South Australia, P.D. Belcher qualified in Pharmacy at the Adelaide University in 1900. He was a relief pharmacist in Port Pirie, South Australia, where he met and married Eunice Williams in 1905. In 1915 he owned the pharmacy at 121 Miller Street, North Sydney, which was unique in having an 11:00pm closing time.

P.D. sold up his pharmacy and enlisted in Sydney in March 1917, and by August of that year embarked on the *HMAT Persic* from Melbourne, bound for India. A large contingent of medical staff including 30 Staff Sergeant Dispensers travelled together on the *Persic*.

P.D was stationed in Deolali, India, in 1917. Deolali was the site of a British Army camp and hospital, located some 100 miles north east of Mumbai. Wounded troops were treated in India rather than being shipped back to England where it might affect morale. Deolali is the source of the English slang term "to go doolally" (mad or insane) and referred to the madness of men waiting for transport back to Britain after finishing their tour of duty.

On his return from war in 1919, P.D. was discharged at his place of enlistment, Sydney. However his family had spent the war years in Adelaide and P.D., now aged 39, was desperate to be reunited with his wife Eunice and daughter Beth, now nine. The State borders had been closed due to the worldwide influenza epidemic. P.D. got as far as Broken Hill, and then smuggled himself over the border in a Cobb & Co coach.

During 1943-44, P.D. was President of the Pharmacy Society. Amongst some of the priceless original manuscripts of P.D. Belcher is a book of his own compounding recipes. In those days the recipes were personal to each pharmacist and closely guarded; however we can assume that during the war effort there was collaboration between chemists. One lasting relic of his war service is P.D's recipe for curry powder (pictured below).

Pictured: Compounding recipe for curry powder, from the personal collection of compounding recipes of Percival Dudley Belcher, with faint annotations by William 'Bill' Carter.

Drug Safety: The Effect on Drug Metabolism by Cytochrome P450

Khai Minh Ngo, Locum Pharmacist
HPS – Alexander Avenue, South Australia

Pharmacokinetic drug interactions, either as drug-to-drug or drug-to-food, have been repeatedly identified as one of many critical factors which influence the practice of modern medicine. One source of drug interactions is associated with the cytochrome P450 (CYP450) system. This is a family of isoenzymes responsible for the biotransformation and metabolism of many drugs and chemicals the body is exposed to. Comprehensive understanding of the CYP450 system and its roles in drug interactions assists health professionals identify and minimise the impact of drug issues concerning drug toxicities, variability of therapeutic effect, and adverse drug reactions.

The Role of Cytochrome P450 Enzymes in Metabolism

CYP450 enzymes play a range of important physiological roles; including the synthesis of cholesterol and its derivatives such as steroids, clearance of foreign chemicals, and drug metabolism. During drug metabolism, fat-soluble substances are biotransformed or chemically modified into more water soluble forms so they can be readily cleared from the system via bodily fluids, such as urine.

Biotransformation carried out by CYP450 enzymes is mainly via oxidation, which predominantly takes place in hepatic tissue and partly in extra-hepatic organs such as the small intestine, lungs, placenta, and kidneys.

It has been found that more than fifty CYP450 enzyme subclasses exist, and 90% of drugs are metabolised by enzymes from the CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 subclasses. Each of the enzyme subclasses have selective binding affinity specific to substrates with very particular molecular structures. Together, the CYP450 enzymes 'super-family' contribute to the body's ability to metabolise a range of chemicals of different shapes and sizes.

CYP450 enzymes are usually under the influence of different regulatory mechanisms. Through these biochemical processes, CYP450 enzyme activities can be induced or inhibited by specific chemical mediators, including endogenous hepatic factors and exogenous factors such as components of medicines or food.

Drug interactions may occur when drug and food components bind to these CYP450 enzymes and change their capacity to metabolise another drug. Alternatively, drug interactions involving CYP450 enzymes also occur when the exogenous components compete with another drug for the same binding site on the enzyme, and subsequently displace and exclude it from the metabolism process. This leaves the displaced drug being ineffectively cleared, and accumulating within the body.

Implication on Drug Interaction

As drugs and food components are known to induce, inhibit, or displace other drugs from binding to an enzyme; it is this physicochemical characteristic which classifies them in literature as either: an enzyme "inducer", "inhibitor", or "substrate".

For example; in the drug interaction between atorvastatin and erythromycin, erythromycin acts as a potent inhibitor of the CYP3A4 enzyme which metabolises atorvastatin. As a result, it causes elevation of the atorvastatin plasma concentration and consequently increases the risk of adverse events or drug toxicity, such as rhabdomyolysis and myopathy.

On the other hand are instances such as where St. John's wort interacts with warfarin. As warfarin is metabolised predominantly by the CYP2C9 enzyme, St. John's wort's inducing effect on this enzyme accelerates the elimination of warfarin, to reduce the anticoagulant blood level and thus increases the risk of thrombosis.

The mechanism associated with each drug interaction, however, is not always straightforward and the clinical implication can vary significantly depending on the influence of many factors related to the drug, patient, and method of administration. For example, sertraline is known to be a mild inhibitor of CYP2D6 at a dose of 50mg, but it can become a potent inhibitor at doses

reaching 200mg, and inhibitory effects usually occur immediately.

Additionally, drug metabolism via CYP450 can vary between different patient ethnic groups, where these enzymes are expressed at different levels according to the genetic makeup of each person, known as polymorphism. Each individual inherits copies of gene encoding for enzymes with varying levels of activity, where they can be "poor metabolisers" (reduced activity), "extensive metabolisers" (normal enzyme activity), or "ultra-rapid metabolisers" (increased activity). Polymorphism in CYP450 enzymes highlights the need for consideration of dose adjustment among different patient groups according to drug response, and suggests the need for genotype testing in future clinical practice to prevent adverse drug effects, or to help identify poor responders.

CYP3A4 and Strong CYP Enzyme Inducer and Inhibitor

Amongst all the CYP450 enzymes subclasses, CYP3A4 is the most abundant CYP enzyme in the body, accounting for 30-40% of the total hepatic CYP content, and is involved in metabolism of numerous drug substrates, of which many have a narrow therapeutic index. Therefore, CYP3A4 is the most common CYP enzyme mentioned in literature regarding drug interactions.

To date, many drugs have been recognised for their effects on particular CYP450 enzymes. Itraconazole, ketoconazole, clarithromycin, erythromycin, nefazodone, ritonavir and grapefruit juice have been reported to cause clinically significant drug interaction due to their strong inhibitory activities on CYP3A4. If co-administered with other CYP3A4 substrates, which have narrow therapeutic windows and potentially life threatening adverse effects, such drug interaction could result in therapeutic crises.

A list of the most clinically significant drugs that affect, or are affected by, CYP450 enzymes and their varying potency, are readily accessed in literature such as the *Australian Medicines Handbook*.

Food-Drug Interaction

Apart from drug-to-drug interaction, certain foods including fruits, vegetables, herbs, spices, and teas have been reported to have the ability to affect the activity of CYP450 enzymes. Grapefruit juice is an example of a food-to-drug interaction due to its strong inhibitory effect on the CYP3A4 enzyme, which also metabolises many drugs such as cyclosporin, felodipine and the statins. Other interactions of a similar mechanism include St. John's wort with cyclosporin and indinavir, or cyclosporin with red wine.

Implication for Prescribing and Therapeutic Monitoring in Practice

As the general population ages and acquires co-morbidities; multiple-drug regimen, or polypharmacy, becomes an inevitable element of existing and future medicinal practice. It is crucial for health professionals to be aware of possible drug interactions and their clinical implication in multiple-drug therapy, and in particular for drugs with a narrow therapeutic window.

Although elimination of the offending agent is the ideal solution to any interaction, this is not always possible. Other appropriate interventions which should be considered include prescribing safe drug combinations, slowly titrating to a response related dose, or close therapeutic monitoring of drug levels and potential adverse reactions.

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Orthostatic Hypotension in the Elderly

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Orthostatic hypotension (OH) is a common condition in the elderly. It is associated with significant risk of morbidity and independently predicts all-cause mortality. It is defined as a decrease in systolic blood pressure (BP) of at least 20mmHg or a decrease in diastolic blood pressure of at least 10mmHg within three minutes of an erect posture (e.g. upon standing), relative to a supine blood pressure reading. OH is most prevalent in, though not limited to, the elderly population; it is characterised by a variety of clinical features, including impaired cognition and speech, disturbed emotion, falls and fractures, and increased risk of cerebrovascular and cardiovascular events. It occurs in approximately 30% of adults over the age of 65, and up to 70% of elderly nursing home residents. In addition to its unpleasant and disabling symptoms, people with OH are more likely to be physically frail which results in decreased functional capacity; a factor that is often overlooked during evaluation of older patients.

Pathogenesis

OH often results as a consequence of inadequate autonomic compensation during postural change. It depends on a combination of mechanisms, such as inadequate intravascular volume, dysfunction of the autonomic nervous system, reduction of venous return, and defective heart rate compensation. Age-related changes that affect normal blood pressure regulation include changes in baroreceptor reflex sensitivity, decreased renal salt and water conservation, and impairment in diastolic filling. These factors contribute to OH, along with the presence of multiple chronic diseases and the combination of various drug therapies.

Aetiology

The causes of OH can be either acute or chronic. Acute OH commonly develops over a short period of time and is more often symptomatic at the onset. It can be caused by adrenal crisis, brady/tachyarrhythmia, myocardial infarction, sepsis, dehydration and some medications. In contrast, chronic OH develops over time and the patient is usually initially asymptomatic. It can result from physiological and pathological causes. Physiological causes include baroreceptor insensitivity, diastolic dysfunction and hypertension. Pathological causes include the central nervous system, brain stem lesions, Lewy body dementia, multiple cerebral infarctions, multiple system atrophy, myelopathy, Parkinson's disease, the peripheral nervous system, amyloidosis, alcoholisms, pure autonomic failure and pernicious anaemia.

Clinical Features

Patients experiencing OH may be symptomatic or asymptomatic. Although a patient may be asymptomatic, OH remains an important risk factor for future falls and syncope, and should be managed where possible. Common signs and symptoms of OH include: lightheadedness, dizziness and confusion, decreased cognition and disturbed speech, weakness and lethargy, visual changes (blurred vision, tunnel scotomas, greying of colours), syncope, palpitations, nausea and a tendency to fall.

Management

Treatment of OH in the elderly can be challenging due to the presence of multiple co-morbid conditions with non-specific signs and symptoms. Instead of aiming to achieve arbitrary blood pressure goals, the aim of treatment should be directed towards reducing the incidence and severity of postural symptoms, correcting underlying causes, improving the patient's functional status, and reducing the risk of complications. Broadly, interventions can be divided into non-pharmacological and pharmacological approaches.

Non-pharmacological Management

Generally, non-pharmacological measures should be the first-line approach to treatment. The first management step involves removing any medication that could contribute to OH. Table 1 lists common drug contributors to OH.

Other non-pharmacological management options include:

- Taking causative medications at bedtime (e.g. antihypertensives)
- Standing or sitting up gradually, especially after prolonged inactivity or bed rest
- Avoiding large carbohydrate meals and limiting alcohol intake
- Ensuring adequate hydration (minimum 1.25-2.50L of fluid per day)
- Sodium supplementation by increasing salt intake or salt tablets
- Abdominal binders and waist-high compression stockings

Therapeutic Class	Therapeutic Subgroup/Drug
Anaesthetics	
Antidepressants	MAO inhibitors, tricyclic antidepressants
Antihypertensives	ACE inhibitors, alpha$_1$-adrenergic antagonists, angiotensin II antagonists, beta blockers, calcium channel blockers, diuretics, vasodilators
Antiparkinsonian agents	Dopamine agonists, levodopa
Antipsychotics	Atypical antipsychotics, chlorpromazine
Narcotics	
Nitrates	Glyceryl trinitrate
Other drugs	Alcohol, marijuana
Phosphodiasterase-5 inhibitors	Sildenafil, tadalafil, vardenafil
Sedatives	

Table 1. Drug classes commonly associated with orthostatic hypotension

Drug Type	Mode of Action	Dosage	Contra-indications	Common Adverse Effects
Fludrocortisone	Synthetic mineralocorticoid. Reduces salt loss and expands blood volume.	Initially 0.1mg daily, increase by 0.1mg weekly. Maximum dose of 1mg daily.	Hypersensitivity, systemic fungal infections	Headache, supine hypertension, congestive heart failure, oedema, hypokalaemia
Midodrine	Peripheral selective alpha$_1$-adrenergic agonist. Increases standing systolic BP through constriction of blood vessels.	Initially 2.5mg three times daily, titrate in 2.5mg dose increments weekly. Maximum dose of 10mg three times daily.	Coronary heart disease, urinary retention, thyrotoxicosis, acute renal failure, phaeochromocytoma	Piloerection, pruritus, paraesthesia, supine hypertension
Octreotide	Somatostatin analogue. Reduces post-prandial hypotension via inhibiting release of gastrointestinal peptides, leading to splanchnic vasoconstriction.	Subcutaneous injection, 25-50microgram half an hour before meals	Hypersensitivity. Use cautiously in patients with diabetes, insulinoma and gastroenteropancreatic tumours.	Nausea, abdominal pain, flatulence, vomiting, hyperglycaemia, hypoglycaemia

Table 2. Pharmacological agents for the management of orthostatic hypotension

- Raising the head of the bed by 10-20 degrees at night
- Exercise programs and physical manoeuvres (e.g. standing with legs crossed, bending forward, squatting, dorsiflexion of feet)

Pharmacological Management

Pharmacological treatment may be indicated when a patient does not respond adequately to non-pharmacological management. Table 2 summarises medications used in treatment of orthostatic hypotension.

In patients who do not respond adequately to non-pharmacological treatment, specific drug therapy may be indicated. Fludrocortisone is a valuable first-line therapy for OH. Should a patient remain symptomatic on fludrocortisone, a sympathomimetic drug such as midorine can be added to therapy. The availability of midodrine in Australia is currently restricted to the *Special Access Scheme*. In the United States, it is the only approved peripheral selective alpha$_1$-adrenergic agonist for the treatment of orthostatic hypotension. It is also approved for use in several European Union countries, including Germany, France, Ireland, Italy and Spain.

Other drugs that have been trialled in the treatment of OH include pyridostigmine, erythropoietin, indomethacin, pseudoephedrine, caffeine, clonidine, dihydroergotamine, desmopressin and yohimbine; however the efficacy and safety of these therapies has not been adequately established. Further large randomised clinical trials are required to support the effectiveness of current therapeutic management options and to identify novel treatment approaches.

Referral to a Specialist

Consultation with a geriatrician should be sought for frail elderly patients and those with multiple co-morbid conditions, including cognitive decline, failure of standard therapy, any symptom-related complications or lack of social support. Referral to a cardiologist is indicated for patients with: uncontrolled supine hypertension despite standard therapy, advanced symptomatic coronary artery disease, severe heart failure, and those with recent onset of tachy/bradyarrhythmias. A neurological consult would be recommended if specialised autonomic testing is required in patients with an unclear diagnosis and progressive autonomic failure.

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Medication Safety and NSQHS Standards

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Introduction

The *Australian Commission on Safety and Quality in Health Care* (ACSQHC), which was formed in 2006, is a government funded commission created with the aim to improve the quality and safety of health care. The *ACSQHC* developed ten *National Safety and Quality Health Service* (NSQHS) Standards which reflect the *ACSQHC's* goals for all health care services to provide a high level of safety and quality of systems.

Background

Issues with the safety and quality of health care in Australian hospitals were identified in several studies during the 1990's. One example was the *1995 Quality in Australian Health Care Study*, which was a review of over 14,000 admissions in 28 hospitals in New South Wales and South Australia.

Of the hospital admissions reviewed, 16.6% were associated with an adverse event that was caused by health care management, and over half of these were considered preventable. From this, and other similar studies, it was estimated that the cost of health care was increased by 15–20% as a result of adverse events.

In 2000, further reviews of health care quality were undertaken, which eventually led to the instigation of reforms in 2005. The reforms saw an agreement between state and federal governments that introduced a national oversight of hospital performance by new independent agencies, including the *ACSQHC* and the *National Health Performance Authority* (NHPA). While the *ACSQHC* focuses on developing a framework for safety and quality, the *NHPA* has a focus of creating and reporting on national performance standards. Prior to the reforms, approximately 98% of hospitals participated in voluntary accreditation programs offered by a number of non-government agencies, including the *Australian Council on Healthcare Standards* (ACHS).

NSQHS Standards

The *NSQHS* Standards define a framework for the provision of high quality health services, and all Australian accredited hospitals must meet these standards. Accreditation includes an independent and external assessment of conformity to the *NSQHS* Standards. Each standard provides a description of the intended outcome and a list of criteria with which to assess if it is being met. There are both core actions and developmental targets within each standard.

The focuses of the ten *NSQHS* Standards are:

1. To ensure the quality and safety of health care is well managed, which includes confirming that the workforce of the health service is appropriately qualified to provide safe and quality care.
2. Providing a framework for interacting with the consumers of health care.
3. Infection control, including antimicrobial stewardship.
4. Medication safety.
5. Provision of measures to ensure accurate patient identification. This includes using at least three patient identifiers to confirm identity before providing any care, therapy or service.
6. Clinical handover systems to ensure there is appropriate documentation and structured communication of patient information.
7. The safe and appropriate use of blood and blood products.
8. The prevention and management of pressure injuries.
9. Recognising and responding appropriately to deterioration of a patient's condition.
10. Fall prevention and management to reduce the harm from falls.

Standard 4: Medication Safety

The *NSQHS* Standard 4: Medication Safety is described as follows:

"Clinical leaders and senior managers of a health service organisation implement systems to reduce the occurrence of medication incidents, and improve the safety and quality of medicine use. Clinicians and other members of the workforce use the systems to safely manage medicines".

When addressing medication safety, it is important to reflect on adverse events in all

settings, rather than focus on events that occur in health care facilities. An estimated 1.5 million Australians experience an adverse medication event each year. As medicines are the most common form of treatment, the incidence of these adverse events is higher than for other health care interventions. These events result in approximately 400,000 visits to general practitioners and 190,000 hospital admissions annually. The estimated cost of hospital admissions related to medication incidents is $660 million.

The *ACSQHC* noted in 2005 that 90% of medication safety problems are due to the systems in place rather than the 10% which are due to the individual. Not only are medication adverse events costly, many are also potentially avoidable. The goal of Standard 4 is to reduce the prevalence of adverse events by providing a system for actively improving safety and quality in the services of health care providers.

There are many aspects to medication safety that are covered in the Standard. Appropriate policies and procedures for medication safety are integral and need to be consistent with national and jurisdictional legislative requirements. The policies and procedures should be regularly and comprehensively assessed and revised to minimise any identified risks.

A health service should have systems in place to verify that clinicians are authorised to prescribe, dispense and/or administer medicines. Medication incidents are a risk to patient safety and therefore must be reported, investigated and reviewed appropriately.

All adverse drug reactions should be reported to the *Therapeutic Goods Administration*.

Taking accurate medication histories, documenting a patient's previous adverse medication reactions and the reconciliation of a patient's current and previous medication lists are also important. This reduces errors by preventing duplication, interaction, allergic reaction, and omission of critical medications.

Health service providers should have the appropriate information resources available to them. The information resources provided should be reviewed and updated to ensure they are relevant.

The appropriate storage and safe distribution of medicines is essential. Incorrect storage of medicines can endanger patients. Another focus within the Standard is high risk medications. Medicines with a high potential for patient harm should be identified and appropriately stored, prescribed, dispensed and administered. Education on each of these high risk medicine groups is available through the HPS Lecture Series Programme.

A commonly used acronym to identify high risk drugs is **A PINCH:**

A – Anti-infectives

P – Potassium and other electrolytes

I – Insulin

N – Narcotics and other sedatives

C – Chemotherapeutic agents

H – Heparin and anticoagulants

It is also important that lists of current medicines are provided to patients and clinicians during clinical handover. Patients need to be given the right information to be able to correctly manage their medications on discharge.

To fully achieve *NSQHS* Standards, the consumer of health services should be included in medication management. This includes clinicians advising consumers and carers about the risks and benefits of medication and their treatment options to enable the patient to make well informed decisions about their care.

Conclusion

NSQHS Standard 4 offers a valuable framework to ensure the safe and quality use of medications by health service providers in Australia. Through standardisation and systemisation, medication adverse events can be prevented. Adherence to all ten *NSQHS* Standards is assessed during hospital accreditation. As Australia's leading pharmacy service provider, HPS Pharmacies has developed programs to assist health care facilities to meet, and surpass, the *NSQHS* Standards. This includes a dedicated Antimicrobial Stewardship program to allow facilities the opportunity to undertake external audits.

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The Stigma of Mental Illness

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Almost half of all Australians will experience a mental health disorder within their lifetime, and one in five Australians aged 16-85 years have experienced mental disorders within the last 12 months. Episodes may come and go throughout a person's life; whereas others may be transient and thus those patients can fully recover. Only 35% of mental health sufferers seek treatment, which is thought to be half the proportion of the population who seek treatment for physical disorders.

Despite the availability of mental health care for Australians, many tend to avoid treatment for a myriad of reasons. Barriers such as attitude, financial concerns and perception, whether self-perceived or society's stigma, lead to avoidance of treatment. Beyond mental health, this lack of treatment may also result in deterioration of physical health and relationships with family, friends and work.

Stigma is defined as "a mark of disgrace associated with a particular circumstance, quality or person". In the context of mental health, stigma refers to the community's misconceptions of mental illness.

Misconceptions can include beliefs that those who suffer from mental illness are dangerous, that sufferers are "all the same", or that they are unfit to work. Inaccurate ideas regarding mental health can be perpetuated throughout the community and reinforced by the media.

A multitude of consequences may occur; sufferers may feel socially alienated, others feel discouraged from seeking health care, and some may face discrimination within their community or workplace, further hindering recovery.

Stigma is of particular importance to those who are in adolescence and early adulthood. There is a high occurrence of mental health issues associated with these age groups; with young people less likely to seek professional help. The stigmatising attitudes surveyed in the *2011 National Survey of Mental Health Literacy and Stigma Report* showed little change from attitudes in the 2003-4 survey. This trend was also demonstrated in a 2007 study which explored the barriers to mental health treatments in rural Australia. The adolescents who participated in this study described the extent and effect of social stigma in their community, resulting from the "gossip networks" which contributed to social exclusion and ostracism. A resultant fear of social stigma negatively influenced their desire to seek help as well as compounding the impact of the illness. In the case of Aboriginal families, the study found fear and mistrust of potentially unwarranted government interventions (e.g. a child being removed from the family) added to the stigma.

The *NSW Consumer Advisory Group* (supported by the *NSW Department of Health*) is lobbying to implement a program similar to one introduced in New Zealand which includes a broad advertising campaign featuring people with mental illness educating the public, the ongoing education of journalists about the effects of discriminatory reporting of mental health, and also monitoring journalist reports.

The role of health care professionals is vital to provide effective treatment to patients. The medical paradigm for treatment has shifted from an authoritative relationship to one of collaboration between client and practitioner, and it is this concordance that is vital to optimise patient outcomes. Patients should be offered respect, empathy, compassion, help to seek support when needed, and a sense of hope, as one of the most disabling aspects of mental illness is the perception of exclusion from ordinary activities and treatment by the community as a whole. Specifically, pharmacists can offer measures to improve patient education and behavioural prompts, as well as monitoring medication use. Patient education involves dispelling misconceptions of mental illness, providing personalised counselling along with written communications (such as consumer medicine information leaflets) and explaining the details regarding the impact of particular medicines. In addition, pharmacists may suggest prompts to manage medicines; whether by incorporating dosing schedules into the daily routine (e.g. taking the medication after breakfast), suggesting

dose administration aids such as blister packs or self-monitoring aids, or positively acknowledging and reinforcing concordance. It is vital to actively ask the patient about the adverse effects of medicines and to explore potential solutions around these effects. For example a day time dose that may be shifted to an evening dose in response to a patient's sedation.

Patients should be directed to useful resources and support organisations such as: *beyondblue, SANE Australia, the Black Dog Institute, Mind Australia,* and *Lifeline*. Focussing on public health, *beyondblue* tailor information for specific population groups to provide easily accessible education, health services and online tools. The *Black Dog Institute* is pioneering diagnosis, treatment and prevention of mood disorders. It also partners with universities, health services and community groups to focus on access to, and running of, education programs. Some organisations also have trained mental health professionals to offer personalised and confidential support through a variety of mediums.

It is important for society to recognise the impact that social stigma has on sufferers. By changing society's perception of mental illness, mental health treatment outcomes can be improved.

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Cetuximab: Management and Prevention of Cutaneous Side Effects

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Cetuximab is an immunoglobulin (Ig) G-1 monoclonal antibody indicated for the treatment of squamous cell carcinomas of the head and neck and KRAS (Kirsten rat sarcoma virus oncogene homologue) wild-type metastatic colorectal cancer. It binds to the epidermal growth factor receptor (EGFR) and inhibits the activation of the tyrosine kinase pathway. The inhibition of this pathway blocks important cell mechanisms such as signal transduction, regulation of cellular activity, and cell division. Inhibition of the EGFR hinders re-epithelisation of the skin during the wound healing process, and decreases antibacterial activity of the epidermis. EGFR inhibition also disrupts the innate immune response of the skin to wound healing. As a result of this, cetuximab reduces skin integrity. Cutaneous toxicities are therefore common during treatment with cetuximab.

A study conducted by Pfeiffer *et al.* of weekly versus biweekly cetuximab demonstrated that patients without skin toxicities had a shorter progression free survival (3.4 months versus 6.2 months; P=0.004) and shorter overall survival (6.3 months versus 9.9 months; P=0.004). These results indicate that the efficacy of cetuximab is correlated to the presence of cutaneous toxicities. There is a distinct correlation between rash severity and patient survival.

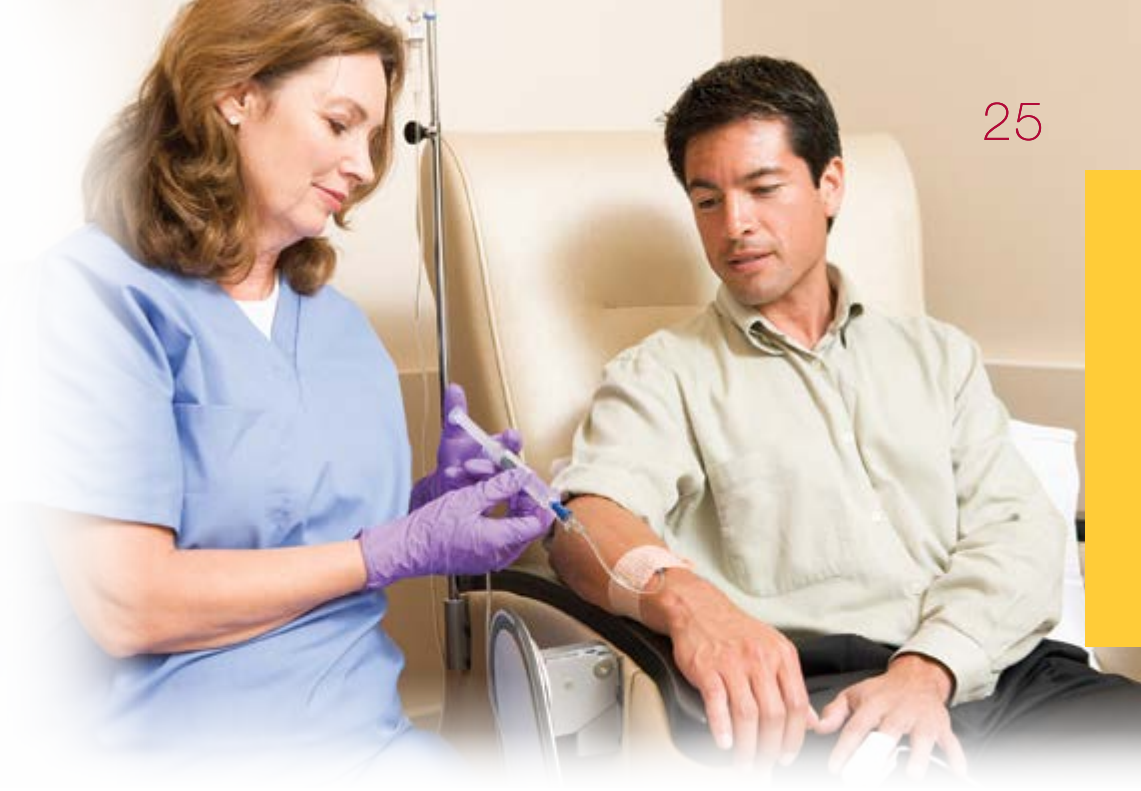
While clinicians may use the presence of rash as a surrogate marker for cetuximab efficacy, this skin toxicity needs to be managed to prevent significant morbidity in patients and the possible cessation of an effective treatment, especially since treatment of rash does not interfere with patient survival. Although cutaneous toxicity may not be life threatening, depending on its severity, it may result in dose reduction or even cessation of treatment. There are four distinct cutaneous manifestations; folliculitis (infection in hair follicles), xerosis (dry skin), paronychia (inflammation of skin bordering toenails or fingernails), and hair changes. These types of cutaneous toxicities are common to all EGFR inhibitors (EGFRI). The recommendations of management may be applied to the entire class.

Folliculitis appears as acne-like papules and pustules that occur on the face, scalp, and upper trunk. It occurs in 85% of patients undergoing EGFRI treatment. 10-20% of patients develop grade 3-4 folliculitis. This acneiform rash appears during the first weeks to months of therapy. Survey results gathered from 110 oncology practices showed that 60% of patients required dose reductions, 75% dose interruptions, and 32% drug discontinuation.

Treatments that may be beneficial include; oral antibiotics (e.g. tetracyclines: minocycline, doxycycline, and erythromycin), topical retinoids, oral isotretinoin, and low-potency corticosteroids. It is important to note that topical retinoids need to be used with caution as they may aggravate the condition by drying the skin. Hydrocortisone 1% is the preferred treatment for pruritus (itch) associated with folliculitis.

Xerosis (abnormally dry skin) manifests between the first and second months of treatment. Xerosis can be managed with the frequent application of moisturisers and the use of soap substitutes. Pruritus associated with xerosis can be managed with systemic antihistamines and oily calamine or 1% menthol in aqueous cream. For more severe cases of xerosis, with fissures, 20% urea cream, liquid Duoderm® or flexible collodion may be beneficial.

Paronychia involves the swelling or inflammation of the nail folds on the fingers and toes. Usually this toxicity manifests at a later stage, six months after therapy. In a study with 152 patients who were undergoing treatment with cetuximab, 27 patients developed paronychia. Prevention of paronychia has been observed with daily use of mild corticosteroid cream and antiseptic soaks of saline, or diluted bleach. Pain and discomfort associated with paronychia may warrant dose changes, however interruptions are generally not necessary. Paronychia management aims to minimise trauma and inflammation, and to prevent infection of the skin bordering the nails.



Hair changes generally occur after 2–3 months: they include trichomegaly (long curly eyelashes), hypertrichosis (increased facial hair), frontal alopecia, and dry brittle scalp hair. When treatment has been discontinued, alopecia tends to resolve.

Despite practice variations and few controlled studies, the *Multinational Association for Supportive Care in Cancer (MASCC) Skin Toxicity Study Group* assembled committees to develop guidelines for the management and prevention of cutaneous toxicities arising from the use of EGFRI, as summarised below.

Prophylactic management of folliculitis is crucial. The high incidence of EGFRI skin rash after two to four weeks of therapy warrants prophylactic management. The *MASCC* guidelines recommend that patients use hydrocortisone 1% cream with moisturiser and sunscreen twice daily. Antibiotics are to be given prophylactically; doxycycline 100mg twice daily for 1–6 weeks or minocycline 100mg daily for eight weeks from EGFRI commencement. Minocycline is less photosensitising then doxycycline, however doxycycline is preferred in patients with renal impairment. The frequent and daily application of vitamin K_1 cream (Pliazon®) is recommended by the manufacturer, Merck Serono, and is included in their Erbitux® (cetuximab) patient pack. This, however, is not recommended in the *MASCC* guidelines as the published reports supporting the use of the vitamin K_1 cream are based on studies without control groups. There is some speculation that the use of minocycline 50mg daily and doxycycline 50mg daily may suffice.

Treatment of acneiform rash includes a potent corticosteroid of the oncologist's choice (in Australia) and clindamycin 1%, whereas the pruritus associated with folliculitis requires only a mild steroid. Systemic treatments include a prophylactic tetracycline (at the doses recommended above). However, isotretinoin at low doses of 20-30mg/day has been reported as beneficial if all other treatments have not been successful.

Prevention of xerosis, as per the *MASCC* guidelines, is not based on randomised clinical trials as none are available. Prevention includes regular moisturising of skin, avoiding soaps, and bathing in tepid water. Treatment measures for mild to moderate xerosis include emollient creams containing urea or colloidal oatmeal. For scaly areas; salicylic acid 6% and zinc oxide (13–40%) is recommended. Medium to high potency steroid creams are recommended for severe xerosis.

To prevent paronychia, frequent use of diluted bleach soaks (0.005% sodium hypochlorite) and the avoidance of irritants is recommended. Treatment of paronychia includes corticosteroids, tetracyclines, antibacterials (according to culture and sensitivities) and biotin for brittle nails. *MASCC* recommendations for paronychia prevention and treatment are based on expert opinions and case reports as there is no evidence to support approved treatments.

Prevention of non-scarring alopecia is not recommended but treatment includes minoxidil 2% or 5% twice daily. Scarring alopecia, however, should be prevented using the same measures used to reduce the inflammation of folliculitis. Use of steroid shampoos are indicated in treatment. To prevent complications from trichomegaly, eyelashes should be trimmed regularly.

Although there are limited documented randomised controlled studies that investigate the cutaneous toxicities of EGFRI use, there are many case reports and data which show that common toxicities occur in a large percentage of patients undergoing EGFRI treatment. The principle of cutaneous toxicity management in cetuximab (and other EGFRI) treatment is to treat early, and fully, for as long as is required to prevent and manage these toxicities without impacting on the patients' outcomes.

References for this article can be found in the online version published in the Knowledge Centre.

To read more on this topic visit the Knowledge Centre online: http://www.hps.com.au

HPS' 2015 Lecture Series Programme

Anne Reeves, Clinical Pharmacist
HPS – Alexander Avenue, South Australia

HPS' network of pharmacies' Lecture Series Programme has been an integral part of the professional services provided to clients throughout HPS' forty years of operation. The Lecture Series Programme offers in-service education sessions which cover topics such as new medicines, side-effects, adverse reactions to medicines and other issues relevant to patient care. They may address medicines from the perspective of an individual medicine or therapeutic class, the management options for disease states, regulatory controls, or the practical aspects of drug calculations, administration techniques and therapeutic monitoring.

The annual program offers a minimum of twelve lectures, with at least one released at the beginning of every month and additional lectures throughout the year, to assist in keeping nursing and medical staff abreast of current trends in pharmaceutical care.

The topics are selected from those suggested by feedback and client surveys, and integrated with a needs analysis conducted by the visiting Clinical Pharmacists. The lectures are then researched and written by one of HPS Pharmacies' 170 pharmacists who may have specialist knowledge, work or interest in the topic. The completed lecture, along with further reading, is made available to all HPS Pharmacies' pharmacists to present to their valued clients.

Your HPS Pharmacies' pharmacist can assist in tailoring a lecture program suitable for your facility, including drawing upon HPS' bank of more than 60 lectures to meet your requirements if a particular topic is not covered by the current program. Attending staff are provided with handouts that include a self-assessment tool to assist their learning process, and may be used to contribute toward their 'Continuing Professional Education' (CPE).

Each lecture can easily be adapted to suit a variety of audiences and group sizes. HPS offers a range of presentation styles from a brief presentation during handover to an in-depth discussion for staff, and can adapt lectures or develop materials for participants who may not have a medical background.

Every edition of *Newsline* includes a *Lecture Series* summary article based on a lecture selected from the current program. These articles, such as *Antimicrobial Stewardship in Australian Hospitals* from the 2014 series, can be found in the Lecture Series section of the Knowledge Centre within the HPS website.

The diverse schedule for HPS' 2015 Lecture Series Programme seen opposite can be downloaded, along with a full list of alternative topics from the HPS Knowledge Centre.

For further information regarding HPS' comprehensive lecture series, please speak to your HPS Pharmacies' pharmacist, Pharmacy Manager, or contact the Regional Operations Manager in your state (details are listed on the inside back cover of this edition of *Newsline*).

To read more on this topic visit the HPS Knowledge Centre online: http://www.hps.com.au

Available From	Topic Title	Topic Summary
1st January 2015	Medications and the Liver	The liver is the principal organ of drug metabolism in the body, therefore any dysfunction or disease may affect how some medications work.
1st February 2015	Basal Bolus Insulin or Sliding Scale Insulin? What's the Big Deal?	A review and look at the new insulin prescribing charts being rolled out across Australian hospitals.
1st March 2015	IV Administration of Medications	A general discussion of the IV adminstraion of medications including what equipment to use, whether or not medications can be mixed, and which may be given as bolus doses.
1st April 2015	Smoking Cessation and the Use of Nicotine Replacement Therapy	A discussion on nicotine dependence and use of nicotine replacement therapy as an aid to smoking cessation.
1st May 2015	Prevention and Treatment of *Pneumocystis jiroveci (carinii)* Pneumonia	A discussion on how *Pneumocystis jiroveci (carinii)* pneumonia (PCP) can be prevented and treated.
1st June 2015	Medication Treatments for Chronic Obstructive Pulmonary Disease	An update on medications used to treat Chronic Obstructive Pulmonary Disease.
1st July 2015	The Role of Phosphate Binders in Renal Failure	A discussion of medications which are used as phosphate binders and how they are used to manage patients with renal failure.
1st August 2015	NSQHS Standard 4 – Medication Safety: Use of the Medication Management Plan	A discussion of NSQHS Standard 4 – Medication Safety, with particular reference to medication management plans.
1st September 2015	Drug Treatment for Prostate Cancer and Disorders	An update on the current drug treatments available for prostate disorders and prostate cancer.
1st October 2015	Drugs With Multiple Indications	This lecture will look at drugs with multiple indications and their dosages.
1st November 2015	Applying Antimicrobial Stewardship in the Treatment of Community Acquired Pneumonia	How the principles of antimicrobial stewardship apply to the treatment of community acquired pneumonia.
1st December 2015	The *Pharmaceutical Benefits Scheme*: What Makes a Valid Prescription?	A discussion on the *Pharmaceutical Benefits Scheme*; schedules of benefits, streamlined authority and telephone authority prescriptions.

Table 1. HPS' 2015 Lecture Series Programme Schedule

Managing Motor Complications in Late Stage Parkinson's Disease

Hamid Juma Mohamed, Clinical Pharmacist
HPS – Modbury, South Australia

Patients with late stage Parkinson's disease (PD) develop several motor and non-motor complications, which dramatically impair their quality of life. These complications include motor fluctuations, dyskinesia, absent or unpredictable response to medicines, falls, dysautonomia, dementia, hallucinations, sleep disorders, depression, and psychosis.

Despite a short plasma half-life of approximately one hour, levodopa's duration of action can last days, independent of plasma concentration. However, the duration of effect reduces (to hours at most) as the disease progresses; a phenomenon strongly linked to the loss of slowly evolving postsynaptic pharmacodynamic changes in the central nervous system (CNS), rather than the plasma concentration at this stage. Patient mobility may fluctuate throughout the day due to dopaminergic stimulation being either inadequate (off-periods) or excessive (peak dose dyskinesia).

Common Motor Fluctuations

(a) Akinesia (motor blocks and freezing) are the most debilitating symptoms of PD. At times, a patient can experience a total loss of movement which may involve hesitation when beginning to walk (start hesitation), or sometimes a sudden inability to move the feet during specific situations, such as turning or crossing busy streets, contributing to falls. Five subtypes of freezing motor blocks are: "start hesitation", "turn hesitation", "hesitation in tight quarters", "destination hesitation" and "open space hesitation".

(b) Morning akinesia (delayed onset of response to first daily dose) may occur due to delayed gastric emptying (gastroparesis), impaired intestinal absorption, pharmacodynamic effects, or other mechanisms which are common in PD and are best managed using strategies to enhance levodopa absorption.

(c) Early morning dystonias are an abnormal tonicity of muscle, characterised by prolonged, repetitive muscle contractions (spasms) that may cause twisting or jerking movements of the body or a body part.

(d) "Off" periods (drug resistance) result from the failure of a dose to induce an "on" period and are often due to gastroparesis.

(e) Diphasic dyskinesia (dyskinesia-improvement-dyskinesia [D-I-D] pattern response): Patients experience dyskinetic symptoms lasting up to half an hour before the levodopa takes effect and dopamine receptors are "switched on". Patients then express no symptoms as the medicine is metabolised, and will again experience over an hour of dyskinetic symptoms after the medicine wears off. There is no one remedy for the "D-I-D response".

(f) Peak dose dyskinesia (improvement-dyskinesia/dystonia-improvement [I-D-I] pattern response): Involuntary movements of the limbs or trunk occur, usually when the plasma levels of levodopa are maximal (peak dose dyskinesia).

(g) On/off phenomenon (random oscillations/fluctuations) are an almost invariable consequence of sustained levodopa treatment, characterised by phases of immobility and incapacity associated with depression, alternating with jubilant thaws. Both pharmacokinetic and pharmacodynamic factors are involved in its pathogenesis.

(h) End of dose dystonia (wearing off) causes painful twisting and cramping of the feet or legs at the end of a dose cycle, such as early in the morning. This is due to inadequate dopaminergic stimulation.

(i) Myoclonus: Sudden, rapid and brief involuntary jerking of muscles or parts of muscles, without any rhythm or pattern, occurring due to various brain disorders.

(j) Akathisia: Motor restlessness ranging from a feeling of inner disquiet, often localised in the muscles, to an inability to sit still or lie quietly. This is a relatively common side effect of antipsychotics, antidepressants (SSRIs), metoclopramide, some calcium channel blockers, dopamine agonists, amphetamine, and buspirone. Symptoms of akathisia are both objective and subjective. Objective symptoms involve movements which usually take the form of shuffling of feet while sitting, and pacing or rocking while standing. Subjective symptoms are feelings of dysphoria that include tension, panic, irritability and impatience.

Management Options

Therapeutic management should have the objective of creating a balance between the benefits and adverse effects of the pharmacological treatments available.

Manipulating the timing and/or dose of medicines can improve motor control, from administering larger and less frequent dose increments, to reducing and overlapping doses *(e*)*. Absorption can be enhanced by crushing or chewing the tablets, using a dispersible formulation, and taking the dose on an empty stomach with a full glass of water *(b, d)*. Using a slow release formulation can extend the duration of action, particularly overnight *(d)*.

Levodopa plasma levels can be adjusted to improve motor control throughout the day using strategies such as introducing slow release preparations, especially for the last dose at night to protect against nocturnal "off-periods" or early morning akinesia *(h)*. They are less effective in treating daytime motor fluctuations. Supplementation with a "kick-start" from a rapid release formulation can prevent morning dystonias *(b)*. Levodopa levels can also be maintained with smaller, more frequent, doses by introducing oral solutions, or continuous duodenal (gel) or intravenous infusions *(b, c, d, f, g, h)*. Alternatively, adding a catechol-O-methyl transferase (COMT) inhibitor (e.g. entacapone) will inhibit the metabolism of levodopa to preserve plasma levels *(e, g, h)*. Decreasing the night-time levodopa dose is recommended for managing myoclonus *(i)*.

Dopaminergic alternatives can augment the dopaminergic effect of levodopa. Gradually introduce or increase a dopamine agonist (e.g. bromocriptine), while potentially reducing the levodopa dose *(a, b, c, d, f, g, j)*. Alternatively, add a longer half-life dopamine agonist, preferable in younger patients (e.g. pergolide, pramipexole, ropinirole or cabergoline). The parenteral dopamine agonist, apomorphine, may be administered subcutaneously as intermittent injections or by continuous infusion *(d, g)*.

Adjuvant medicines, such as amantadine, propranolol, fluoxetine, buspirone or clozapine, may be considered. Amantadine can cause nightmares, anticholinergic adverse effects and livedo-reticularis, a skin condition. It should be avoided in patients with hallucinations or dementia. If used, the last dose should be given before mid-afternoon *(j)*.

Also consider adding: monoamine oxidase (MAO)-B inhibitors (e.g. rasagiline, selegiline), benzodiazepine (e.g. clonazepam) *(i, j)*, baclofen (which should be carefully introduced to avoid aggravation) *(c)*, or gabapentin *(j)*. Anticholinergic medicines may be added or reduced *(e)*, and botulinum toxin may be used for selective denervation *(c)*.

The adjuvant drugs recommended for the management of end-of-dose dystonias *(h)* reduce the "off time", the levodopa dose, and improve *Unified Parkinson Disease Rating Scale* scores, but at the cost of increased dyskinesias and numerous other side effects.

Non-drug and other adjunctive managements that may be considered include deep brain stimulation *(d, e, g)* or a drug holiday *(g)*. Regular exercise and shedding excess weight are useful during the early stages of the disease to maintain good muscle tone and reduce any impediments to movement other than those caused by the disease.

Stereotactic functional neurosurgery is very effective in younger patients with severe motor fluctuations that do not have obvious cognitive impairment, and are poorly controlled with medicines. Assessment by a movement disorder specialist, with or without neuropsychological assessment, is recommended prior to referral to a neurosurgeon.

Supportive care, including physical and rehabilitative interventions by allied health professionals have key roles in the later stages of disease. Physiotherapists and occupational therapists can assist in: developing gait modifications (e.g. tapping, rhythmic commands, stepping over objects and rocking), balance retraining, providing instructions regarding compensatory strategies which emphasise the use of external cues to help initiate movement, or how to break down complex movements into simpler sequences. Speech therapists can improve speech clarity and volume, and alleviate swallowing difficulties through careful assessment and treatment. Dietitians can provide useful guidance, particularly to reduce intake of protein and antacids *(b)*, which may affect the pharmacokinetics of medicines. Hence, it is imperative to have an integrative approach in managing motor complications in late stage Parkinson's Disease.

** The italicised letters within brackets on this page refer to the Common Motor Fluctuations discussed on page 28.*

References for this article can be found in the online version published in the Knowledge Centre.

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