It has been ten years since HealthPACT was established to develop horizon scanning techniques for the identification and assessment of new and emerging technologies.

New technologies can contribute to one third of the increase in healthcare costs and it is important to obtain value and appropriateness with new devices, diagnostics, prostheses and procedures. HealthPACT has extended its role to assist with the implementation and evaluation of new devices in the absence of an organised clinical trial system for non-drug technologies. HealthPACT has established links with industry and inventors as the development of a biomedical industry is important in our society.

HealthPACT continues to search for more effective ways of identifying new technologies. We value our links with state and territory technology committees, health services and the hospital clinician networks. Our work program is in continuous review and we welcome nominations for new and emerging technologies which have the potential to impact service planning, workforce and infrastructure.

On behalf of HealthPACT, I would like to wish our colleagues in the health technology industry a safe and happy New Year.

Best Regards,

Brendon Kearney
Chair of HealthPACT
Autologous blood injection

HOW IT WORKS
The injection of a patient’s own (autologous) blood into a region that is affected by a soft tissue injury may promote the body’s natural healing process. Soft tissue injuries, such as plantar fasciitis (chronic heel pain), lateral epicondylitis (tennis elbow), patella tendinosis (jumper’s knee) and other forms of tendinopathy are characterised by poor blood supply that may contribute to the slow healing process. Platelets in the blood carry platelet-derived growth factors which, when introduced into an injured region, may stimulate a healing response through the recruitment of stem cells, increased vascularisation and the production of collagen.

A small amount, approximately 2-3 mL, of blood is withdrawn from the patient, mixed with a local anaesthetic and re-injected into the area around the affected tissue, usually under ultrasound guidance. The main side effects observed are pain and bruising at the site of the injection, which may persist for 1-2 weeks. During this period, patients are advised to avoid strenuous or excessive use of the injured region prior to beginning a physiotherapy regime. Autologous blood injections are inexpensive and simple to acquire and prepare; application confers minimal trauma, and there is little risk for immune-mediated rejection.

THE EVIDENCE
Three randomised controlled trials were included for assessment of the safety and effectiveness of autologous blood injection compared to injection with a corticosteroid, or corticosteroid and placebo in patients with lateral epicondylitis. Two of the 3 included RCTs reported safety outcomes for the treatment of autologous blood injections in patients with lateral epicondylitis; while one observed no side effects of the treatment, the other reported significantly more pain after autologous blood injection compared to corticosteroid.

In this same study, 2 patients treated with corticosteroid reported skin atrophy, with no reports in patients who received autologous blood. No instances of tendon rupture were reported. Other safety concerns associated with the treatment may include bruising and infection; the studies included did not report on these outcomes.

In terms of effectiveness, each of the studies included for the lateral epicondylitis indication reported significantly improved outcomes compared to baseline regardless of the treatment group (autologous blood, corticosteroid) and patients receiving placebo (saline) also reported improvements compared to baseline. The two studies that compared injections of autologous blood to corticosteroid observed significantly better improvement in patients who were treated with blood, particularly at time points beyond one month. No significant differences were observed between the treatment groups in the study that compared autologous blood to steroid or saline injections.

FUTURE STEPS
Based on the level and availability of evidence for multiple indications, in addition to the diffusion of autologous blood injections within Australia, HealthPACT agreed the technology should be monitored for 24 months.

Written by Arlene Vogan and Stefanie Gurgacz (ASERNIP-S). A full copy of this brief can be accessed via the HealthPACT website: http://www.health.qld.gov.au/healthpact

REFERENCES
**BNP to guide heart failure treatment**

Since July 2008, a MBS item number has existed for the “Quantitation of BNP or NT-proBNP for the diagnosis of heart failure (HF) in patients presenting with dyspnoea to a hospital Emergency Department”. This Brief assessed the current evidence for the use of BNP assays to monitor and guide treatment in patients already diagnosed with HF.

**HOW IT WORKS**

The physiological effects of the brain natriuretic peptides are varied including inhibition of neural-hormonal over-activation, relaxation of vascular and pulmonary smooth muscle, and the inhibition of cardiac hypertrophy and ventricular fibrosis. In addition, the peptides may cause lipolysis, increase the permeability of the endothelial vasculature and reduce intravascular volumes. The level of BNP or NT-proBNP in the plasma directly relates to the severity of HF symptoms and is often associated with a worse patient prognosis. BNP has been demonstrated to be a strong predictor of cardiovascular and all-cause mortality. As such, levels of BNP may act as a prognostic tool that is independent of, and more accurate than, NYHA class and left ventricular ejection fraction (LVEF). It has been postulated that regular, serial measurements of BNP may be used as a tool to guide HF therapy, in particular, using BNP measurements as a guide to achieving optimal pharmacotherapy by titrating therapies. By optimising therapy, it is hoped that the number of re-hospitalisations of HF failure patients will be reduced, further reducing overall costs associated with HF.

**THE EVIDENCE**

Several RCTs and 2 meta-analyses of RCTs were reporting on the use of BNP or NT-proBNP for guiding treatment of HF were identified for inclusion in this Brief. The meta-analysis by Felker et al included 6 studies, all of which, bar the STARBRITE trial, were included in the meta-analysis of 8 studies by Porapakkham et al. Only the results from this latest meta-analysis are reported here. All-cause mortality was lower in patients whose post-discharge HF treatment was guided by the use of BNP compared to those patients who received usual care (RR= 0.76, p=0.003). A sub-group analysis found that all-cause mortality in patients <75 years with HF treatment guided by BNP testing was lower (RR= 0.52, p=0.005) compared to patients treated with usual care, a difference that was absent in those aged >75 years (RR = 0.94, p = 0.70). There was no significant difference between the intervention and usual care groups for the outcome of all-cause hospitalisation (RR = 0.82, p = 0.12) or for survival free of any hospitalisation (RR = 1.07, p = 0.58). However, these last three outcomes were not reported by all studies.

A relatively small cost-effectiveness analysis concluded that BNP-guided treatment of HF patients was more cost-effective than usual care. It is unclear if the results of this Austrian analysis would be generalisable to Australia or NZ, however base costs were similar, albeit lower, to those used in the Australian health system.

Anecdotal evidence suggests the MBS item number that describes the use of BNP tests for the diagnosis of heart failure is being used “off-label” to monitor the treatment of heart failure patients. Since the publication of the 2007 MSAC assessment a wealth of good quality RCTs have been published that describe the use of BNP or NT-proBNP assays to monitor therapy in heart failure patients. In addition, an on-going New Zealand study is currently being conducted that intends to enrol the largest patient group to date and offers the potential for a cost-effectiveness analysis being conducted that is relevant to the Australasian health system.


**REFERENCES**

Basic fibroblast growth factor for ear perforations

The tympanic membrane is a thin layer of tissue which moves in response to variations in air pressure; its vibrations are transmitted to the cochlea through the ossicular chain stimulating the inner ear. Disruption of the tympanic membrane can compromise a patient’s hearing and perforation compromises the barrier between the outer and middle ear, increasing the risk of otitis media (middle ear infection). 1

HOW IT WORKS

The technology is a new method for closing tympanic membrane perforations using a gelatin sponge impregnated with basic fibroblast growth factor (b-FGF) as a patch material. The aim of the procedure is to encourage healing of the perforation by providing the conditions necessary for tissue regeneration (cells, scaffolds and chemical mediators which regulate cell growth and proliferation). The b-FGF stimulates proliferation of epidermal and connective tissue cells and the gelfoam acts as a sustained release substrate for the b-FGF.

The intervention consists of a gelfoam sponge soaked in b-FGF which is placed at the perforation and sealed in position with fibrin glue. Local anaesthesia is administered and the perforation margin is trimmed before the sponge is placed. In paediatric patients the procedure may be performed under general anaesthesia.2

THE EVIDENCE

Three studies were included, one which assessed both the safety and effectiveness of b-FGF for repair of tympanic membrane perforations and two which considered effectiveness only.1,2,3

Limited safety data related to the procedure were identified; in the single study reporting safety data there were eight patients who experienced 16 complications within a three-month follow-up period. The complications included serious otorrhea (n=8), slight retraction of the tympanic membrane (n=6) and aural fullness (n=2). In a second study which reported only infection, one patient in the treatment group experienced infection as compared to nine patients in the control. No evidence to indicate that the procedure is associated with severe safety concerns was identified.

The evaluation of efficacy is limited by the lack of comparative data, as no studies reported the relative effectiveness of b-FGF treatment compared to myringoplasty. The included studies found perforation closure rates associated with the procedure are over 90%; however, only 2 studies included a control group and in one the control sample size was 10 patients.

FUTURE STEPS

Based on the level and availability of evidence, and the potential for widespread uptake of this technology, it is recommended that the technology be monitored for 24 months with a view to obtaining evidence from the Australian trial currently underway.

Written by Robyn Lambert and Stefanie Gurgacz from ASERNIP-S.

A full copy of this brief can be accessed via the HealthPACT website: http://www.health.qld.gov.au/healthpact

REFERENCES

Liver disease is a broad term used to cover a range of diseases of various aetiologies, which can either be congenital (e.g. Wilson’s disease, porphyria, pyrosinemia) or acquired (e.g. hepatitis A, B and C, cirrhosis, non-alcoholic fatty liver disease, and hepatocellular carcinoma). Due to the significant variation in liver disease aetiology, no individual test is available through which to diagnose and assess the nature and extent of all liver diseases.

**HOW IT WORKS**

Breath tests measure exhaled metabolites of labelled substrates that have been ingested and metabolised by the liver; and the concentration of these metabolites in the breath act as a surrogate marker for liver function. Labelled methacetin-¹³C is rapidly metabolised by the cytochrome P450 enzyme system, releasing ¹³C-labelled CO₂ which is exhaled and collected at the bedside via a nasal cannula. Molecular correlation spectroscopy is used to measure the percentage dose recovery (PDR) of ¹³C and the cumulative PDR (cPDR). The higher the PDR and cPDR, the closer the liver function is to normal.

**THE EVIDENCE**

Three studies were included in this assessment, however only the results from the largest study are summarised here. To access the full Brief please refer to the HealthPACT web site.

The accuracy of BreathID® in assessing the degree of liver fibrosis and inflammation was assessed in patients with untreated hepatitis C (HCV) infection and normal serum alanine aminotransferase (ALT) levels who had undergone a liver biopsy in the last 12-months and compared to 100 age- and sex-matched healthy volunteers. Baseline levels of ALT and aspartate aminotransferase (AST) were significantly different ($p<0.01$) between the HCV and control groups. Based on the results of the pre-test liver biopsy, patients were grouped according to histological activity index (HAI), fibrosis scores of $\leq 2$ (non-significant, $n=50$) and $>2$ (significant, $n=50$), and HAI necro-inflammatory scores of $\leq 4$ (low, $n=32$) and $>4$ (high, $n=68$). PDR and cPDR were measured at 10, 15, 20, 30 and 60 minutes for all patients. For comparison, values were divided into low- and high-inflammatory groups and significant and non-significant fibrosis groups.

To determine whether use of the MBT test negates the need for a liver biopsy, the authors applied an algorithm that accounted for breath test parameters and baseline patient characteristics. Based on this algorithm, 67% of liver biopsies performed in the patient group could have been avoided. To assess for reproducibility of results, 42 healthy volunteers and 11 HCV patients each undertook between 2 and 6 additional tests. In both groups, inter-test variability of $\leq 13\%$ was observed for PDR peak height ($95\%$ CI, 0.11-0.15).

**FUTURE STEPS**

Based on the scant evidence available at present, and the observation that four registered clinical trials will be completed by the end of 2012, HealthPACT recommended that the technology be monitored for 24 months.

Written by Heath White from ASERNIP-S.

A full copy of this brief can be accessed via the HealthPACT website:


**REFERENCES**

Obstructive sleep apnoea (OSA) is characterised by repeated episodes of pharyngeal obstruction during sleep, including airway collapse (apnoea) or narrowing (hypopnoea), resulting in recurrent airflow cessation. Immediate symptoms of OSA include loud snoring, choking and gasping, and disrupted sleep. OSA is also associated with excessive daytime sleepiness, cognitive impairment, and cardiovascular and metabolic morbidities, resulting in a significant increase in mortality. During deep sleep, the muscles of the throat relax, leading to a reduction in airflow. In OSA, complete relaxation of these muscles may cause the tongue to prolapse into the throat, causing the cessation of airflow. Tongue prolapse may be due to diminished neuromuscular activity in the genioglossus muscle. The genioglossus muscle can be targeted through the electrical stimulation of its motor nerve, the hypoglossal nerve. The branches of this nerve that innervate the genioglossus are predominantly motor fibres, and as such, stimulation of this nerve has the ability to activate the muscle with minimal sensory feedback. 

HOW IT WORKS

Hypoglossal nerve stimulation systems consist of an implantable neurostimulator that delivers an electrical current to the hypoglossal nerve by a stimulation lead. Stimulation is synchronised with respiration sensing leads that measure changes in breathing. The device is surgically implanted under general anaesthesia, with the stimulating lead placed on the main trunk of the hypoglossal nerve. The neurostimulator is implanted in an infra-clavicular subcutaneous pocket, and the respiratory sensing leads are placed between the external and internal intercostal muscle (Figure 1). 

THE EVIDENCE

Although 4 case series describing the use of hypoglossal nerve stimulation were included in this brief, only the results from Eastwood et al are summarised in this bulletin. For full results please access the complete Brief on the HealthPACT web site. This case-series was conducted at 4 Australian sites and used the Apnex HGNS® System for the treatment of OSA. Patients (n=21) underwent surgical implantation of a hypoglossal nerve stimulation system. Therapy was initiated 30 days post-implant, with daytime and overnight studies used to determine the effectiveness in reducing OSA severity. Two serious adverse events were observed (9.5%): the device was explanted in one participant due to a procedure-related haematoma and infection while the second required an additional procedure for lead replacement due to a cuff dislodgment. A 3rd patient elected for explantation of the device in order to proceed with an alternative surgical treatment. A postoperative reduction in AHI to less than 20 events/h and a > 50% postoperative reduction in AHI was observed in 12/21 participants after 6-months of therapy. Overall, AHI decreased from 43.1 at baseline to 19.1 (-56%) at 3-months (p<0.001), and 19.5 (-55%) at 6-months (p<0.001). Additionally, participants with BMI less than 35 kg/m² were observed to have a lower AHI at six months post-implant, compared to those with a BMI greater than 35 kg/m². Compliance with the therapy was high, with use on 89 ± 15% of nights, at an average of 5.8 ± 1.6 hours per night.

FUTURE STEPS

Based on the limited level of evidence available, and the use of the device at an experimental level only, HealthPACT recommended that the technology be monitored for 24 months.

REFERENCES

Surgical site infections (SSIs) are a predominant cause of post-operative morbidity and mortality, and can range from superficial infections, where skin and subcutaneous tissue are affected; to deep tissue or systemic infections and sepsis. Standard practice to reduce the incidence of SSIs by patient skin preparation with an appropriate antiseptic agent, which can reduce skin bacterial counts by 80%, however some organisms persist.

InteguSeal® is a cyanoacrylate-based microbial sealant that may further decrease rates of SSI incidence. The sealant can be incorporated into current pre-operative skin preparation practices, with application following standard skin sterilisation methods. Cyanoacrylates polymerise on contact with moisture and proteins on the outermost layer of the epidermis forming a solid film. Upon application, InteguSeal® forms a continuous, yet breathable barrier that immobilises the bacteria that survive pre-operative preparation, and subsequently prevent migration of microbes into the incision site.

A large, multi-centre RCT assessed the safety and effectiveness of InteguSeal® for the prevention of SSIs in CABG patients. Patients were randomised to receive standard skin preparation followed by the use of the InteguSeal® microbial sealant (n=146) or to receive standard skin preparation alone (control n=147). In the InteguSeal® group, sternal and graft surgical sites were prepared with standard preparations, followed by the application of the sealant. After 3-minutes the sealant was considered dry and surgery commenced. Microbiological samples were collected from both incision sites during pre-skin preparation, post-incision and at the end of the CABG procedure and assessed for total bacterial burden.

Adverse events were experienced in 11 InteguSeal® patients (7.5%) and in 16 (10.9%) control patients, mostly related to SSIs. The average bacterial counts were highest in the pre-skin preparation samples, and lowest in the post-incision samples for both groups, with no significant between-group differences. There was a significant difference observed between the intervention and the control group in the post-CABG samples at the sternal site (intervention 0.58 CFU/mL, control 0.83 CFU/mL, p=0.039), with a trend observed at the graft site (intervention 0.19 CFU/mL, control 0.34 CFU/mL, p=0.057). Mean bacterial counts in both groups increased from post-incision to post-CABG; however, the increase observed in the intervention group was significantly less than that in the control group at both incision sites (sternal site: intervention 0.37 CFU/mL, control 0.57 CFU/mL, p=0.047; and graft site: intervention 0.09 CFU/mL, control 0.27 CFU/mL, p=0.037). SSIs developed in 9 (6.2%) patients in the intervention group and 14 (9.5%) patients in the control group (NS).

Based on the outcomes, the quality of available evidence and the potential diffusion of use in Australia, HealthPACT recommended that the technology be monitored for 24 months.
Neonatal screening for lysosomal storage disorders

In Australia, newborn screening for selected genetic disorders using dried blood spots (DBS) does not include screening for lysosomal storage disorders (LSDs). Several studies have been published that implemented pilot screening for LSDs to assess the practicality and appropriateness of including these disorders in neonatal screening panels.1

LSDs comprise more than 50 serious, progressive diseases that arise due to an inherited dysfunction in the lysosome. Loss-of-function mutations in one or more of the hydrolytic enzymes, or other integral lysosomal proteins, can lead to substrate accumulation and storage within the lysosome.2 Progressive lysosomal substrate deposition can occur in cells throughout the body.1 This accumulation can result in the deterioration of cellular and tissue function, and the dysfunction of vital organs, muscles and neurons.2,4 Most patients have a decreased lifespan and significant morbidity.2 Treatment is generally directed towards symptomatic care of secondary complications; however, for some LSDs, haematopoietic stem-cell transplantation and enzyme replacement therapy are emerging as promising treatments.1,2 Due to the progressive nature of these disorders, the effectiveness of these therapies relies heavily on early detection and treatment.

Screening for LSDs typically involves the collection of DBS, with subsequent enzyme activity analysis, using such technology as electrospray ionisation tandem mass spectrometry (ESI-MS).1 ESI-MS enables the simultaneous screening of several enzyme activities related to LSDs from DBS samples and high-throughput, multiplex assays have been developed to simplify and expedite workflow.5

THE EVIDENCE

From the primary study by Mechtler et al1, nation-wide neonatal screening for several LSDs using ESI-MS was technically feasible. More accurate confirmation of an LSD could be obtained after repeated biochemical screening and genetic testing. In this study, the combined incidence of the 4 LSDs screened for was higher than expected (1 per 2,315 births). This was in agreement with other screening studies for single LSDs that also noted that neonatal screening produced higher incidence rates than previously recorded clinical diagnosis rates.6,9 These studies detected a high proportion of mutations linked with late-onset disease symptoms. Individuals with such mutations are likely to appear asymptomatic in early years, and without neonatal screening would only be identified later in life or not at all. Whilst LSD screening is technically effective, and holds no more safety risk than current screening programs using DBS, the introduction of an expanded nation-wide neonatal screening program for LSDs is associated with both economic and ethical issues. The value of detecting an LSD at birth is clear when favourable outcomes are dependent on early initiation of treatments. More ethical issues surround the detection of LSDs where treatments are less effective, or where the likelihood and timing of symptom development is unknown.2 Economic considerations include the downstream costs associated with confirmatory diagnosis, specialist clinical consultant input, genetic counselling services and participation in paediatric metabolic programs following a positive diagnosis.

FUTURE STEPS

Based on the increasing availability of evidence for population-wide neonatal LSD screening, and the economic and ethical issues surrounding this technology, HealthPACT recommended that the technology be monitored for 24 months.

Written by Ms Karen Humphreys (ASERNIP-S)

REFERENCES

Pleurx® catheter system

Pleural effusion refers to the build-up of abnormal amounts of fluid in the pleural space due to excess production or decreased absorption of fluid. Effusions result in a flattening of the diaphragm, dissociation of the pleura, and reduced ventilation. Malignant cells in the pleural fluid and/or parietal pleura indicate the presence of malignant pleural effusions (MPE) and advanced disease. MPE is most commonly symptomatic and patients experience shortness of breath, coughing, and pain on breathing.¹

HOW IT WORKS

The Pleurx® tunneled pleural catheter system was developed to control symptomatic, recurrent MPE and trapped lung syndrome. The Pleurx® device and similar catheters are referred to as in-dwelling pleural catheters and are soft, flexible catheters placed in the pleural space and tunneled through the sub-cutaneous tissue. IPCs are inserted under local anaesthetic and light sedation, most often in the outpatient setting. Attachment of a vacuum drainage bottle facilitates drainage and re-expansion of the lung and the catheter may remain in situ until death. Fluid may be drained as required, by patients, and in the home setting. The catheter may be removed if the patient experiences spontaneous pleurodesis.² A disadvantage associated with the device is the duration of treatment as the catheter may remain inserted for extended periods of time, causing unease or exposing the patient to the risk of infection. For patients receiving an IPC, accessibility to appropriately trained staff from a number of specialties for follow-up and removal of the catheter (if necessary) should form a part of their management strategy.³

THE EVIDENCE

One systematic review and one RCT were selected for inclusion in this technical brief, however only the results from the RCT⁵ are included here.

Patients with MPE were randomised to receive either a Pleurx® catheter (n=94) or pleurodesis with doxycycline (n=43). Early in-hospital morbidity (fever, pneumothorax) occurred in 6 (14%) and 10 (11%) patients in the pleurodesis and Pleurx® groups, respectively. One patient in the Pleurx® group experienced hypercapnic respiratory failure secondary to oversedation and no procedure-related deaths occurred. The median hospitalisation time (the time from randomisation to discharge), for patients in the Pleurx® arm was significantly shorter than for patients in the pleurodesis arm (1 day versus 6.5 days; p=0.0001).

Treatment failure was defined as recurrence of effusion after initial control and occurred in 12 (13%) and 6 (21%) in the Pleurx® and pleurodesis groups, respectively. All 6 patients in the pleurodesis group experienced failure within 30 days. In the Pleurx® group, recurrence was due to loculations in 7 patients (58.3%). In 2 patients, recurrence occurred after initial spontaneous pleurodesis and in a further 2 after catheter occlusion. Replacement of the catheter after occlusion resulted in spontaneous pleurodesis in one patient. One patient did not have a determined cause of recurrence. Improved quality of life was similar in both groups at 30, 60 and 90 days post treatment.

FUTURE STEPS

Based on one RCT and a systematic review consisting of poor quality level IV evidence it is recommended that the Pleurx® catheter be monitored for 48 months. However, recently published evidence is available for the comparable Rocket Medical™ IPC, including the data from the trial in Western Australia, which may warrant further investigation.

Written by Robyn Lambert and Stefanie Gurgacz (ASERNIP-S).

A full copy of this brief can be accessed via the HealthPACT website: http://www.health.qld.gov.au/healthpact

REFERENCES

Objective: To develop and apply a novel method for scanning a range of sources to identify existing health care services (excluding pharmaceuticals) that have questionable benefit, and produce a list of services that warrant further investigation.

Design and setting: A multiplatform approach to identifying services listed on the Australian Medicare Benefits Schedule (MBS; fee-for-service) that comprised: (i) a broad search of peer-reviewed literature on the PubMed search platform; (ii) a targeted analysis of databases such as the Cochrane Library and National Institute for Health and Clinical Excellence (NICE) “do not do” recommendations; and (iii) opportunistic sampling, drawing on our previous and ongoing work in this area, and including nominations from clinical and non-clinical stakeholder groups.

Main outcome measures: Non-pharmaceutical, MBS-listed health care services that were flagged as potentially unsafe, ineffective or otherwise inappropriately applied.

Results: A total of 5209 articles were screened for eligibility, resulting in 156 potentially ineffective and/or unsafe services being identified for consideration. The list includes examples where practice optimisation (ie, assessing relative value of a service against comparators) might be required.

Conclusion: The list of health care services produced provides a launchpad for expert clinical detailing. Exploring the dimensions of how, and under what circumstances, the appropriateness of certain services has fallen into question, will allow prioritisation within health technology reassessment initiatives.