



ANZHSN Bulletin

'New health technologies identified through the Australia and New Zealand Horizon Scanning Network (ANZHSN)'

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Below: Singapore
(Source: Compliments of Linda Mundy)



From the Chair's desk

Dear Colleagues,

HealthPACT has secured funding for the 2009/10 Financial Year. There are governance changes which place HealthPACT as a subcommittee within the Australian Health Ministers' Advisory Committee structure reporting to the Clinical, Technical and Ethical Principal Committee (CTEPC). HealthPACT will retain links with the Medical Services Advisory Committee (MSAC) and continue to have its Secretariat with the Department of Health and Ageing. The past and ongoing support from the Department of Health and Ageing has been essential to HealthPACT's functioning.

The HTAi Sixth Annual Meeting was held in Singapore in June. After Singapore, the largest number of registrants came from Australia. This reflects the strength of HTA

in Australia with Australians contributing significantly to the Scientific Programme, to associated groups such as INAHTA and Euroscan and to the governance of HTAi at board level. The meeting was very successful. The next HTAi Annual Meeting will be held in Dublin in June 2010.

The future for HealthPACT is positive. The stronger links to all jurisdictions within the AHMAC structure will empower the work programme. Comments on the work programme are invited and will be considered by HealthPACT at its next meeting on 28 August 2009.

Professor B J Kearney

Chair, HealthPACT



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Department of Health and Ageing



Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

Rapid testing and targeted population screening for *Helicobacter Pylori*: Executive Summary

Although a large proportion of all gastric cancers are associated with *H pylori* infection, not all *H pylori* infected individuals will go on to develop cancer; however it has been suggested that 60-80 per cent of gastric cancers could be prevented by *H pylori* eradication. In developing countries in Asia and South America, *H pylori* infection is associated with poor hygiene and high levels of infection (70-80% of *all* individuals are infected), and therefore rates of gastric cancer, are high. In Western countries, with improved hygiene, rates of *H pylori* infection have declined (10-20% infection rates) and accordingly rates of *H pylori* associated gastric cancer have also declined.

Numerous diagnostic methods are available for the detection of *H pylori* including non-invasive tests: rapid stool antigen test (enzyme-linked immunosorbant assay or immunochromatographic tests), urea breath test or serology. Invasive tests include the gold standard endoscopy followed by histology, endoscopy followed by culture or the rapid urease test. Rapid *H pylori* diagnostic tests are intended to provide a swift, accurate, non-invasive and inexpensive means of identifying individuals currently infected with *H pylori* which ideally would be able to be used in a point-of-care context in clinics or a general practitioner's office.

Diagnostic

Effectiveness values, compared to the reference standard histology, of the various immunochromatographic HpSA tests (ICTs) varied depending on the brand of test used and age of population tested. Sensitivity ranged from a poor 33 per cent to 100 per cent in individuals aged ≤ 45 years. The best sensitivity reported for an adult population not stratified according to age, was 83.8 %. Specificity ranged from 55 to 100 per cent. Overall, accuracy of the ICT HpSA tests ranged between 50-93 per cent. Of concern is the high number of false negatives that occurred with the use of the majority of the ICT HpSA tests (range 16-66%). However, most studies using ICT HpSA tests reported *low* false positive numbers, indicating that a relatively small number of patients would receive inappropriate treatment.

Reported sensitivity values were consistently higher for the ELISA HpSA tests compared to the ICTs. Sensitivity and specificity of the ELISA HpSA tests compared to histology ranged from 87-95 and 67-100 per cent, respectively. Diagnostic accuracy of the ELISA HpSA tests was also consistently higher when compared to the ICT HpSA tests (range 87-93%).



Above: Electron micrograph of *Helicobacter pylori*
(Source: <http://en.wikipedia.org/wiki/File:EMpylori.jpg>)

Although it would appear that HpSA tests are not as accurate as UBT, they are as, or more cost-effective than UBT for the diagnosis of *H pylori*. In addition, for patients with dyspepsia, it appears that there is little difference in the cost-effectiveness of the two strategies of either empirical treatment with proton pump inhibitors or *H pylori* test-and-treat strategy. In addition, there appears to be little difference in the cost-effectiveness of the two non-invasive tests used: UBT or HpSA. However this situation may change with the falling prevalence of *H pylori* infection.

Screening

H pylori is a *necessary* but *not sufficient* causal factor for gastric cancer and therefore it has been suggested that a screening program for *H pylori* would be able to detect asymptomatic but infected individuals *before* they have developed atrophic gastritis. By treating these individuals with an appropriate antibiotic regime and eradicating the *H pylori* infection, it is anticipated that their risk of developing symptoms of dyspepsia, peptic ulcer disease or gastric cancer would be markedly reduced or eliminated.

There are no clinical guidelines for the screening or management of *H pylori* infection in Australia or New Zealand. However, the Asia-Pacific guidelines *do not* recommend screening for *H pylori* in populations considered to be at low-risk of gastric cancer, such as Australia and New Zealand.

A large community-based Danish study randomised controlled trial compared a screening to a no-screening strategy and compared rates of dyspepsia at 5-year follow-up. *H pylori* positive individuals (17.5%) in the screening arm were offered eradication

Rapid testing and targeted population screening for *Helicobacter pylori* (continued...)

therapy. After analysis of data, including only those individuals followed-up for the five years, there was an *insignificant decrease* in the rates of visits to a general practitioner due to dyspepsia (from 3.1% to 2.8%) and the number of sick leave days due to dyspepsia (from 2.2% to 1.9%) in the screened group but a *significant* ($p < 0.001$) increase in both rates in the unscreened group (2.5% to 3.1% for GP visits and 1.6% to 2.5% for sick leave days).

The most recent screening cost-effectiveness study to be published used a Markov model which evaluated the economics of a population *H pylori* screening programme, and the use of various diagnostic techniques within this strategy, for the prevention of gastric cancer. Although UBT was more sensitive and specific than HpSA and serology, the most cost-effective strategy, depending on the willingness-to-pay threshold values, was either no screening or screening with HpSA tests.

It would appear in populations with a relatively low prevalence of *H pylori* infection, that a *targeted*, rather than a population screening strategy would be more effective for the resolution of

dyspepsia symptoms and for the reduction in the costs associated with treating the condition.

In summary, rapid HpSA stool antigen tests are not as sensitive nor as specific as a urea breath test, however the ICT HpSA tests are relatively cheap, easy to perform in a clinic setting and give an instantaneous diagnosis. An advantage of HpSA tests is that unlike most *H pylori* diagnostic test, cessation of antibiotic and proton pump inhibitor treatment is not necessary before testing. HpSA tests appear to be a cost-effective option when compared to UBT in a “test-and-treat” scenario for patients presenting with symptoms of dyspepsia. The long term effect on rates of gastric cancer of screening for *H pylori* infection has yet to be established.

Written by Linda Mundy, Annette Braunack-Mayer and Janet Hiller (AHTA)

For a full reference list see www.horizonsscanning.gov.au

Tumour treating fields for patients with glioblastoma multiforme

Glioblastoma multiforme (GBM) a grade IV glioma and is the most common and aggressive type of glioma. Patients have a median survival rate of less than 12 months, and a five year survival rate of less than 5% (Chandana et al 2008; Germano et al 2008; Louis et al 2007).

HOW IT WORKS

The Tumour Treating Fields (TTF) device (NovoCure Ltd., Haifa, Israel) delivers low-intensity, intermediate-frequency, alternating electric fields to treat cancer. The electric fields are delivered via electrodes placed onto the patient's shaved skin, and treatment is applied for 2-4 weeks (Schroeder et al 2008). TTF has two modes of action: arrest of cell proliferation and destruction of dividing cells. As only mitotic cells would be destroyed, TTF is thought to be highly specific for cancer (Schroeder et al 2008; Kirson et al 2004).

TTF has been promoted as an attractive treatment option for GBM as none of the present treatment modalities may be

considered curative (Brandes et al 2008) as surgery, chemotherapy and radiation therapy only aim to improve the patient's quality of life and extend survival. Proponents of TTF note that it may have further value through reducing the length of hospital stay as patients do not need to remain in the clinical setting whilst treatment takes place. This also allows patients living in remote areas to return home during treatment. TTF has been depicted as a well tolerated and pain-free, which is an advantage over existing treatment modalities. In addition to this, TTF may be an adjuvant therapy to chemotherapy. It has been proposed that TTF may enhance the effects of chemotherapy without an associated increase in treatment toxicity (Kirson et al 2009).

THE EVIDENCE

Two studies by Kirson et al (2007 and 2009) reported on a total of 20 patients with GBM, divided into two groups. Group 1 (n=10) had recurrent GBM treated with TTF following failure of maintenance chemotherapy. To assess the progression free survival in these 10 patients, the authors made comparisons to a

Tumour treating fields for patients with glioblastoma multiforme (continued...)

matched group of concurrent control patients (n=18) who received salvage chemotherapy at recurrence. Group 1 received continuous TTF treatment until disease progression or for a maximum of 18 months. Meanwhile, group 2 (n=10) consisted of patients who were at least 4 weeks post radiation therapy who were treated with TTF combined with maintenance standard chemotherapy. To assess the progression free survival in these patients, the authors made comparisons to a matched group of concurrent control patients (n=32) who received chemotherapy only. Group 2 received continuous treatment for an average of one year. Overall survival in all 20 patients was compared to matched historical control data. Four 4 electrodes were used to deliver TTF (200 kHz, 0.7 V/cm fields). In the 2009 study, there were no device-related serious adverse events, and the only treatment-related related adverse event was dermatitis. Elevated liver enzymes were also consistently reported but were attributed to anti-epileptic drug usage. Two patients had non-treatment-related partial seizures. In the 10 patients who received TTF with chemotherapy (group 2), the combination did not increase chemotherapy-related adverse events.

Kirson et al (2007) noted that patients treated with TTF exclusively (Group 1 in Kirson et al 2009) had substantially longer median time to disease progression relative to historical controls (26.1 weeks (range 3-124 weeks) vs. 9.5±1.6 weeks). Meanwhile, the progression-free survival at 6 months in TTF patients was 50% vs. 15.3±3.8% in historical controls. Two TTF patients were still progression free at study closure. The median overall survival of TTF treated patients was 62.2 weeks (range 20.3-124.0 weeks) vs. 29.3±6 weeks in historical controls. Kaplan Meier estimates indicated that the 1-year survival rate for TTF treated GBM patients is 67.5%. The TTF resulted in one complete response (10%) which was tumour free 10 months after treatment ceased. Also, one patient (10%) had a partial response that was still responding 7 months after treatment ceased. Both patients were still progression free after more than 2 years from the commencement of treatment. One patient (10%) had a minimal response while four patients (40%) had stable disease for over 4 months before progressing. No data were supplied for the remaining three patients.

Kirson et al (2009) reported no unique outcomes for group one, but did report upon group two (patients treated with TTF and chemotherapy). The median progression free survival of the combination treated patients was 155 weeks vs. 31 weeks for concurrent controls treated with maintenance chemotherapy alone, 50% (5/10) of group 2 patients were progression free at the time of study publication. The median overall survival of

combination treated patients was greater than 39 months vs. about 14.7 months for concurrent controls treated with maintenance chemotherapy alone. At the time of the study publication 80% of combined treatment patients were alive.

Another study by Salzberg et al (2008) reported results narratively, stating that patients with GBM did not respond to the TTF treatment, however no effectiveness data was reported. The authors attributed this failure to the short treatment duration of 4 weeks, compared with 12 and 18 months reported in other cohorts.

FUTURE STEPS

Based on the limited evidence available, the effectiveness of TTF remains unproven. There is insufficient evidence to conclusively state if TTF has a positive impact upon increased patient survival, as all studies had small patient numbers. Although one study found that time to progression increased with TTF from 9.5 weeks to 26.1 weeks, this outcome was not assessed in a prospective control group. It is recommended that TTF technology is monitored for 24 months, and that any further applications of this technology should be noted.

Written by Caryn Perera (ASERNIP-S)

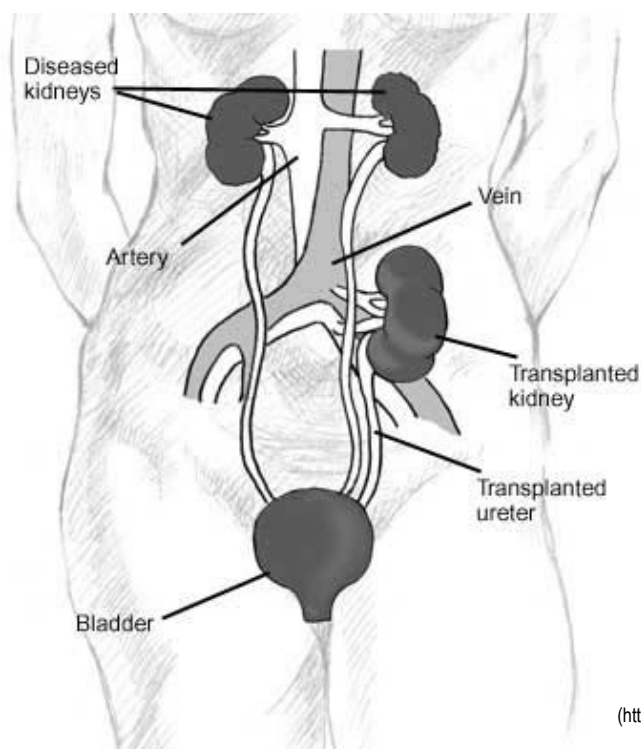
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Positive crossmatch kidney transplantation: Executive Summary

There is currently a severe shortage of available donor kidneys for patients with end stage renal disease. The average waiting time for these patients is four years. For sensitised patients with preformed antibodies against the human leukocyte antigens of their potential donors (positive crossmatch patients), the potential donor pool is much smaller and the waiting times can be much longer. In an attempt to expand the possibilities of increasing the donor pool for these patients and reducing their waiting times, positive crossmatch kidney transplantation using pre-emptive desensitisation techniques has been developed.

Positive crossmatch kidney transplantation was developed following the discovery that plasmapheresis and intravenous immunoglobulin administration are able to rescue patients who develop a positive crossmatch after transplantation. The technique involves the pre-transplant desensitisation of sensitised, positive crossmatched patients with the aim of achieving a negative crossmatch or sufficient reduction in sensitisation to proceed to transplantation. Currently, there exists two commonly used protocols to perform positive crossmatch kidney transplantation, a high-dose intravenous immunoglobulin based protocol and a plasmapheresis with low-dose intravenous immunoglobulin protocol.



Source: US National Institutes of Health
(<http://en.wikipedia.org/wiki/File:Kidtransplant.jpg>)

From the retrieved studies there is some evidence suggesting that reasonable successful desensitisation rates are attainable using either desensitisation protocol. Once desensitised and transplanted, the evidence indicates that both protocols offer similar graft outcomes to one another. However, when compared to negative crossmatch patients who do not require desensitisation, graft rejection occurs more frequently in desensitised patients, regardless of the protocol. In terms of kidney function, there appears to be no difference between the different desensitisation protocols or with negative crossmatch patients undergoing kidney transplantation without desensitisation.

The included studies highlighted the potential role that the degree of sensitisation prior to undergoing desensitisation may play in determining not only the occurrence of successful desensitisation but also in post-transplant graft outcomes. Factors including the level of donor specific anti-human leukocyte antigen antibodies and transplant history were noted in various studies as playing a role in outcomes such as desensitisation and rejection rates.

Overall, the currently available evidence on positive crossmatch kidney transplantation suggests encouraging results for patients who would otherwise not have the possibility of receiving a kidney transplant. Despite this however, positive crossmatch kidney transplantation faces substantial challenges before the technique can be more widely adopted, namely the determination of an optimal desensitisation protocol and determination of long term graft outcomes for desensitised patients receiving kidney transplantation.

Written by Luis Zamora and
Deanne Leopardi (ASERNIP-S)

For a full reference list see www.horizonscanning.gov.au

Hypertonic saline therapy for cystic fibrosis

Cystic fibrosis is a recessive genetic condition caused by defects in the Cystic Fibrosis Transmembrane Regulator (CFTR) gene. CF affects the function of several organs including the lungs, pancreas, intestines, and liver. The CFTR gene is responsible for salt transport across cell membranes and as a consequence of the genetic defect; the mucus of people with CF is thick and viscous. This leads to poor clearance of mucus in organs such as the lungs and consequent repeated infections and blockages eventually resulting in loss of lung function. The degradation of organ function can lead to a shorter life expectancy (Cystic Fibrosis Australia 2009).

HOW IT WORKS

Although it is not fully understood, CF is thought to affect the liquid layer that lines the air exposed lung tissues. The defective CFTR gene may lead to an excessive reduction in this liquid layer, reducing the clearance of mucus. This can then block airways and acts as a promoter for lung infections, both of which lead to decreased lung function over time and eventual lung failure resulting in death. Hypertonic saline (concentrations may range from 4-6%) is thought to increase the volume of this liquid layer and hence undo the effects of the faulty CFTR gene, although this is currently speculation. Pharmaceutical hypertonic saline is administered using widely available commercial nebulisers in the patient's home or clinical settings (Enderby & Doull 2007).

THE EVIDENCE

A study of 164 CF patients was conducted as a parallel, double-blinded trial in which subjects (6 years of age or older) were randomised to the experimental group, inhaling 4 ml of 7 per-cent hypertonic saline, or the control group, inhaling 4 ml of 0.9 percent saline, twice daily for 48 weeks. Both groups were treated with a bronchodilator before inhalation. Subjects continued their normal course of treatment in addition to the hypertonic saline, the randomisation algorithm attempted to correct for differences in treatment between the experimental and control groups. The primary outcome was change in lung function. There was no significant improvement in the primary outcome between the experimental and control arms. However, there were several significant improvements in hypertonic saline arm subjects as measured by secondary outcomes such as decreases in the frequency of pulmonary exacerbations, reduced antibiotic use for exacerbations, and reduced absenteeism from work or school. Although the

primary outcome was not met, there was an absolute difference between the hypertonic saline and control arms but due to variability in both arms the difference did not reach significance. In light of the safety, low cost of hypertonic saline treatment the authors conclude that it is an effective additional therapy (Elkins et al 2006).

A pilot study (n=13) assessed if there were any negative outcomes to a hypertonic saline treatment in infants and young. The subjects were all given a sequential treatment regimen consisting of a throat swab for microbiologic assessment, a baseline assessment of pulmonary function, administration of a bronchodilator, a second assessment of pulmonary function, hypertonic saline administration, and a third assessment of pulmonary function. There was no significant difference in the markers of tolerability assessed before or after hypertonic saline treatment. These markers included lung function, respiratory symptoms, respiration rate, heart rate, oxygen saturation, and microbiologic yield from the throat swab. The only side effect was coughing in 3 infants during hypertonic saline inhalation, which resolved within five minutes (Subbarao et al 2007). A similar study by Dellon et al (2008) in eight infants (4 months to 3 years old) and seven preschoolers (4 years to 7 years) found no change to lung function. The authors concluded that there were no significant issues with administering hypertonic saline to children and young infants.

FUTURE STEPS

The use of hypertonic saline for the treatment of cystic fibrosis patients appears to be routine in a number of Australian jurisdictions, including Queensland and Western Australia, therefore HealthPACT has recommended that further assessment of this technology is no longer warranted.

Written by Adrian Purins (AHTA)

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Health technology disinvestment

Tests, drugs, clinical practice



Southern Health, in conjunction with the Victorian Department of Human Services, invites you to a national workshop to discuss decision-making around 'disinvestment' in health

An interactive day of presentations, case-study analyses and discussion aimed at tackling issues related to 'disinvestment' in health settings.

Presentations from:

- Centre for Clinical Effectiveness, Southern Health
- Centre for Health Economics, Monash University
- Adelaide Health Technology Assessment, University of Adelaide

Thursday 27 August 2009

Venue

Royal Australasian College of Surgeons
Level 2 Training Area
250-290 Spring Street, Melbourne
8:30am—4:30pm
Catering provided

For further information or to register your attendance, contact Luisa Chaves on phone (03) 9096 1410 or email luisa.chaves@dhs.vic.gov.au

Program details will be available at www.health.vic.gov.au/newtech

No registration fee, places limited

RSVP 14 August 2009

Southern Health

Perspectives on 'disinvestment'

Most new health technologies and clinical practices are assessed for safety, effectiveness and cost effectiveness before introduction. However, there are many procedures in current practice that do not meet these criteria or have been superseded.

Cessation or restriction of potentially harmful, clinically ineffective or cost-inefficient practices has the dual advantage of improving patient care and allowing for a more efficient use of scarce resources. This approach, also known as 'disinvestment', has the potential to increase total health benefits without increasing spending.

Realising that 'disinvestment' does not stand alone, but is part of a continuum of decision-making, this workshop will explore issues around 'disinvestment' of health technologies and clinical practices from three perspectives:

- Health service decision-makers
- Health economists
- Health policy researchers

In conjunction with:

A Victorian
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www.health.vic.gov.au/newtech
Department of Human Services

Other New and Emerging Technologies

The following additional technologies were considered by the Health Policy Advisory Committee on Technology (HealthPACT) in June 2009.

- [MRI for diagnosis of rheumatoid arthritis](#) [evidence update]

Further information on the health technologies included in the Bulletin can be accessed on the following link:

<http://www.horizonscanning.gov.au>



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Health Technology
Assessment



PRODUCTION NOTES

The ANZHSN Bulletin is published by Adelaide Health Technology Assessment (AHTA) on behalf of the Health Policy Advisory Committee on Technology (HealthPACT) and funded by the Australian Government Department of Health and Ageing.

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