

## Shorter courses of antibiotics safe for patients with hospital-acquired pneumonia

Patients with hospital-acquired pneumonia and ventilator-associated pneumonia – which account for 20–25% of hospital-acquired infections – should be treated with shorter courses of antibiotics, according to new guidelines from the Infectious Diseases Society of America and American Thoracic Society (Kalil et al, 2016).

Created by a multidisciplinary panel led by infectious diseases, pulmonary and critical care specialists, the guidelines also recommend that each hospital develop an antibiogram, a regular analysis of the strains of bacteria causing pneumonia infections locally as well as which antibiotics effectively treat them. When possible, this should be specific to the hospital's intensive care unit patients.

Kalil AC, Metersky ML, Klompas M et al (2016) Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis pii: ciw353* (doi: 10.1093/cid/ciw353)

## Increased risk of cancer before and straight after diabetes diagnosis

Individuals with diabetes may have an elevated risk of developing cancer before and immediately after a diabetes diagnosis. A team from the University of Toronto looked at cancer incidence in more than 1 million adults at various time points (Lega et al, 2016).

People with diabetes were 1.23 times more likely to have been diagnosed with cancer in the 10 years before a diabetes diagnosis compared with individuals without diabetes. Cancer incidence was also significantly higher in persons with diabetes within the first 3 months after diagnosis, but not after this.

Lega IC, Wilton AS, Austin PC, Fischer HD, Johnson JA, Lipscombe LL (2016) The temporal relationship between diabetes and cancer: A population-based study. *Cancer* (doi: 10.1002/cncr.30095)

## Care for patients undergoing high-risk emergency bowel surgery inconsistent, finds NELA report

Lack of consistent care for patients undergoing high-risk emergency bowel surgery may be negatively affecting patient outcomes and placing major strain on scarce NHS resources, according to a joint national report led by the Royal College of Anaesthetists (NELA Project Team, 2016).

The National Emergency Laparotomy Audit (NELA) report highlights that the annual cost of ward care alone for patients undergoing high-risk emergency bowel surgery is in excess of £200 million, but reports that improvements in care and length of hospital stay have already led to an estimated £22 million savings since the first NELA report was published last year.

Commissioned by the Healthcare Quality Improvement Partnership as part of the National Clinical Audit Programme, the NELA report analyses the care received by more than 20 000 emergency bowel surgery patients treated in NHS hospitals in England and Wales between December 2014 and November 2015.

Analysing patients' short-term survival, the report found that 1 in 9 patients died within 30 days of surgery, but that risk of death ranged from under 5% to over 30%, depending on the patient's condition at the time of surgery. The 30-day mortality rates for individual hospitals were in the range expected given the number of patients and the range of conditions treated, but the report shows substantial variation in the delivery of care against pre-existing national standards.

Professor Mike Grocott, Chair of NELA and Council Member of the Royal College of Anaesthetists said: 'Shortfalls in the perioperative care of these patients before, during and after major surgery may be negatively affecting patient outcomes and use of resources.

He continued: 'There is still much work to be done and it is vital that, clinicians, hospital managers and commissioners of healthcare examine these data to determine why standards are not always met and how improvements can be made. This will lead to better care and efficiencies that will benefit both patients and the NHS.'

Although the proportion of patients receiving a formal risk assessment before bowel surgery has increased from 56% to 64% over the last year, there remain large differences



Professor Mike Grocott, Chair of NELA, Professor of Anaesthesia and Critical Care, University of Southampton, and Consultant in Critical Care Medicine, University Hospital Southampton NHS Foundation Trust, Southampton

in standards of care between hospitals. Rectifying this will require greater engagement between clinicians, health-care managers and commissioners. Investing in resources to bring about improvement and the delivery of higher quality care is also likely to be cost effective, as demonstrated by the estimated £22 million of savings to the NHS since the first NELA report in 2015.

To combat the variation in the levels of care provided across NHS hospitals, the report makes 12 recommendations to health commissioners and providers, to help them move their provision to meeting these standards in over 80% of patients. Currently many hospitals are meeting these standards for 60–70% of patients.

Dr Liam Brennan, President of the Royal College of Anaesthetists, said: 'While today's report highlights significant variation in care for patients who undergo emergency bowel surgery, it has also identified several areas in which NHS clinical teams have implemented recommendations from the 2015 NELA patient report. The acceptance of these recommendations has enabled hospitals to adhere more closely to relevant standards, thereby provide better patient care – and for this they should be commended.'

NELA Project Team (2016) *Second Patient Report of the National Emergency Laparotomy Audit*. Royal College of Anaesthetists, London

## Certolizumab pegol maintains efficacy in axial spondyloarthritis to 4 years

Janet Fricker

The effectiveness of certolizumab pegol was maintained in patients with axial spondyloarthritis over 4 years, reports a phase III trial (van der Heijde et al, 2016). The study, presented at the European League Against Rheumatism (EULAR) meeting, held in London from 8–11 June, found no new safety signals for long-term use.

Axial spondyloarthritis is a chronic inflammatory disease primarily characterized by inflammation of the sacroiliac joints and spine, causing chronic back pain. Certolizumab pegol is a monoclonal antibody to tumour necrosis factor alpha (TNF- $\alpha$ ).

In the RAPID-axSpA trial, involving 315 patients with active axial spondyloarthritis, treatment with certolizumab pegol was double blind and placebo controlled for 24 weeks, dose blind to week 48 and open label to week 216. Results have already been reported out to week 24, but it is important to know whether benefits are maintained over long periods.

Professor Désirée van der Heijde, from Leiden Medical Centre, Leiden, The Netherlands, reported that the proportion of patients with axial spondyloarthritis randomized to certolizumab ( $n=218$ ) achieving the ASAS20 and ASAS40 at week 24 was 68.3% and 51.8% respectively, which was

maintained in the extension study at week 216 at 54.1% and 44.0% respectively.

When divided according to patients with radiographic and non-radiographic axial spondyloarthritis, benefits remained consistent. Some clinicians have previously held non-radiographic axial spondyloarthritis to be a self-limiting disease, suggesting that symptoms disappear without treatment.

‘For clinicians, these data show that efficacy is good after 4 years of treatment. The fact that response rates were very similar in patients with radiographic and non-radiographic disease sends an important message that non-radiographic axial spondyloarthritis is not a self-limiting disease,’ commented Professor van der Heijde.

In a separate phase III study, also reported at EULAR, Dr Philip Mease, from The University of Washington, Seattle, showed that long-term efficacy of certolizumab pegol was maintained in patients with psoriatic arthritis out to week 216 (Mease et al, 2016).

Mease PJ, Fleischmann R, Wollenhaupt J et al (2016) Certolizumab pegol for the treatment of psoriatic arthritis: 4-year outcomes from the RAPID-PsA trial. *Ann Rheum Dis* 75(Suppl2): 608 (doi: 10.1136/annrheumdis-2016-eular.3192)

van der Heijde D, Dougados M, Landewé R et al (2016) Certolizumab pegol for the treatment of axial spondyloarthritis: 4 year outcomes from the RAPID-axSpA trial. *Ann Rheum Dis* 75(Suppl2): 803 (doi: 10.1136/annrheumdis-2016-eular.3142)

## Gender may affect outcomes of corneal transplant

A study of patients undergoing corneal transplants indicates that subtle differences between men and women may lead to poorer outcomes for a woman who has received a cornea from a male donor. The findings (Hopkinson et al, 2016) suggest that gender matching may be beneficial to try and reduce the risk of failure and rejection in patients undergoing corneal transplantation.

The research investigated whether donor and recipient gender incompatibility influences corneal transplant rejection and failure up to 5 years post-transplant.

‘These findings are most likely a result of H-Y antigen incompatibility associated with the male Y chromosome,’ explained Professor

Stephen Kaye, University of Liverpool.

‘Females do not have a Y chromosome so there is no H-Y incompatibility from female donors to male patients. This effect, however, is not reciprocated when the roles are reversed, that is, when male donors are transplanted to female recipients.’

He noted that further studies will be necessary to confirm this and to justify potential allocation of corneas from male donors to male recipients and those from female donors to either female or male recipients.

Hopkinson C, Romano V, Kaye R et al (2016) The influence of donor and recipient gender incompatibility on corneal transplant rejection and failure. *Am J Transplant* (doi: 10.1111/ajt.13926)

### Premature babies not receiving lifesaving care

Fewer than 60% of premature babies born in 11 European countries receive a package of four simple, widely available, evidence-based care measures known to improve survival, found an observational study (doi: 10.1136/bmj.i2976).

### Prevalence of and risk factors for active tuberculosis in migrants

Applicants for long-term visas who were screened for tuberculosis before entering the UK were included in a population-based cross-sectional study (doi: 10.1016/S1473-3099(16)00072-4). Factors strongly associated with an increased risk of bacteriologically confirmed disease at screening were self-report of close or household contact with an individual with tuberculosis and being an applicant for settlement and dependant visas.

### Hospital-at-home safe alternative to hospital admission for over 65s

An evidence review from the University of Bristol found that alternatives to acute hospital care, e.g. hospital at home or admission to a local community hospital, are safe for elderly patients with conditions such as chronic obstructive pulmonary disease, heart failure, pulmonary embolism and pneumonia. However, those with stroke should be treated in specialist stroke services.

### Degrading hyaluronan improves progression-free survival in patients with metastatic pancreatic cancer

The investigational agent PEGPH20 is an engineered enzyme which temporarily degrades hyaluronan, a glycosaminoglycan which accumulates around tumours, including pancreatic, breast, lung, colon and prostate. In animal models, PEGPH20 facilitates delivery of co-administered anticancer agents.

In a phase II study, 135 patients with metastatic pancreatic cancer were randomized to PEGPH20 in combination with nab-paclitaxel and gemcitabine (PAG arm;  $n=74$ ) or nab-paclitaxel and gemcitabine alone (AG arm;  $n=61$ ).

Median progression-free survival was 9.2 months in the PAG arm vs 6 months in the AG arm (hazard ratio 0.46, 95% confidence interval 0.15–1.40). The median duration of response was 8.1 months in the PAG arm vs 3.7 months in the AG arm.

Hingorani S, Bullock A, Wilson W (2016) Final analysis of stage 1 data from a randomized phase 2 study of PEGPH20 plus nab-paclitaxel/gemcitabine in stage iv previously untreated pancreatic cancer patients, utilizing ventana companion diagnostic assay. Poster no PD-006

### Internal radiation more effective in patients with larger metastatic colorectal liver tumour burden

Metastatic colorectal cancer patients with baseline liver tumour burdens  $\geq 12\%$  treated with mFOLFOX6 and selective internal radiation therapy achieved greater depth of response than those receiving chemotherapy alone, reports a German study (Heinemann et al, 2016).

Selective internal radiation therapy, which involves injecting yttrium-90 labelled coated resin microspheres into the hepatic artery via a catheter, allows liver tumours to be selectively irradiated.

In the SIRFLOX study, 530 patients with previously untreated metastatic colorectal cancer were randomly assigned 1:1 to mFOLFOX6 ( $\pm$  bevacizumab) plus selective internal radiation therapy or mFOLFOX6 ( $\pm$  bevacizumab) alone. Although selective internal radiation therapy did not influence progression-free survival at any site, it delivered a 7.9-month prolongation of progression-free survival in the liver.

In the current analysis, Dr Volker Heinemann and colleagues from the Ludwig-Maximilian University, Munich, developed the depth of response analysis where shrinkage of up to five target liver tumours was tracked until



Dr Volker Heinemann, Director of the Comprehensive Cancer Center, Ludwig-Maximilian University, Munich, Germany

reaching the shortest length or 'nadir'. They identified patients from the SIRTEX study with baseline tumour loads  $\geq 12\%$  ( $n=245$ ) and tumour loads  $\leq 12\%$  ( $n=239$ ).

For patients with  $\geq 12\%$  tumour burden, depth of response was 77.5% for mFOLFOX6 ( $\pm$  bevacizumab) and selective internal radiation therapy compared to 57.2% for mFOLFOX6 ( $\pm$

bevacizumab) ( $P=0.003$ ). In contrast, for patients with  $\leq 12\%$  tumour burden the depth of response was 72.5% for mFOLFOX6 ( $\pm$  bevacizumab) and selective internal radiation therapy vs 80.6% for those receiving mFOLFOX6 ( $\pm$  bevacizumab) ( $P=0.763$ ).

'The greater depth of response ... following SIR-spheres Y-90 resin microspheres, together with the prolonged progression-free survival in the liver, are very encouraging and increase our anticipation for the survival data we hope to see in 2017,' said Dr Heinemann.

Heinemann V, Hazel GA, Sharma NK et al (2016) Evaluation of depth of response within a volumetric model in patients with metastatic colorectal cancer: Results of the SIRFLOX study. *Ann Oncol* 27(Suppl 2): ii123 (doi: 10.1093/annonc/mdw198.14)

### Regorafenib promising second-line treatment in hepatocellular carcinoma

Regorafenib, an oral multikinase inhibitor, significantly improved overall survival in patients with hepatocellular carcinoma who had progressed during treatment with sorafenib, reported the RESORCE trial.

'The improvement in overall survival seen with regorafenib signals the addition of a potential option for patients with advanced hepatocellular carcinoma,' said principal investigator Dr Jordi Bruix, head of the Barcelona Clinic Liver Cancer, University of Barcelona, Spain.

In the phase III study, 573 patients

with intermediate or advanced stage hepatocellular carcinoma previously treated with sorafenib were randomized 2:1 to 160 mg oral regorafenib ( $n=379$ ) or placebo ( $n=194$ ) once daily for 1–3 weeks of each 4-week cycle, in addition to best supportive care.

Patients taking regorafenib achieved a median overall survival of 10.6 months vs 7.8 months for placebo plus best supportive care (hazard ratio=0.62, 95% confidence interval=0.50–0.78,  $P<0.001$ ). Median progression-free survival was 3.1 months in

patients taking regorafenib vs 1.5 months in the control group (hazard ratio=0.46, 95% confidence interval=0.37–0.56).

Dr Bruix added that analysis of biomarkers would reveal whether certain subgroups of patients might be likely to derive greater benefits from the treatment.

Bruix J, Merle P, Granito A et al (2016) Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: results of the international, randomized phase 3 RESORCE trial. *Ann Oncol* 27(suppl 2): ii140–ii141 (doi:10.1093/annonc/mdw237.03)

## The need for psychological support among dermatology patients is not being met

Realizing that their standard approach to patients was not efficient enough at recognizing those patients in need of psychological support, the Severe Eczema and Psoriasis Team at St. John's Institute of Dermatology, St Guys' and St Thomas' NHS Foundation Trust, London, redesigned their practice. The team used a tripartite approach first developed by the IMPARTS team, led by Professor Matthew Hotopf, which integrates mental and physical health care in research, training and clinical services. They developed a system whereby iPads are used to survey patients with pre-selected and validated questionnaires relevant to their condition, while waiting for their appointment. This information is then automatically uploaded to their electronic patient record.

The questionnaire results are used to alert doctors to any potential emotional wellbeing issues and automatically suggest treatments or referral pathways that may be appropriate for the patient.

The team found that 71% of their patients, who were subsequently diagnosed with major depressive illness using the new system,

and 88.6% with anxiety, were previously unrecognized as having mental health problems.

Professor Catherine Smith, consultant dermatologist within the Severe Eczema and Psoriasis Team, said: 'This rigorous and systematic approach to providing holistic care within our team has reaped huge benefits for our patients, who previously might have had unrecognized morbidity. Before evaluating our service and introducing this new approach, we considered that we were already providing holistic care.'

She added: 'Identifying the high needs of our patient population motivated us to fully integrate psychological support with treatment of the physical symptoms of skin disease throughout the visit to our service. We improved training for all staff, from our receptionists to our consultant dermatologists, and implemented internal care pathways that ensure the mental wellbeing of the patient is monitored and treated according to their needs. By taking this methodical approach we were also able to quantify and justify the need for a full-time clinical health psychologist on staff.'

## Bacteriophages turbo-charge *Pseudomonas aeruginosa* evolution in patients with cystic fibrosis

Patients with cystic fibrosis suffer from lifelong lung infections caused by *Pseudomonas aeruginosa*. These infections worsen patient health and limit life expectancy. Over the years of the infection, the bacteria evolve to become better adapted to the lung environment, becoming very difficult to treat.

A team of scientists from the Universities of Liverpool, Salford and York evolved populations of the bacterium *P. aeruginosa* with or without bacteriophages in a growth medium designed to replicate the sputum in the lungs of patients with cystic fibrosis. They then tracked evolutionary change in the bacterium using genome sequencing (Davies et al, 2016).



Dr Chloe E James, Lecturer in Medical Microbiology, School of Environment and Life Sciences, University of Salford, Salford

The researchers found that bacteria with bacteriophages evolved faster to adapt to life in sputum, because the bacteriophage jumped into the bacterium's DNA, increasing the number of useful mutations that natural selection could use.

Commenting on the findings, Dr Chloe James, lecturer in Medical Microbiology at the University of Salford, said: 'We now know that these bacteriophages can speed up evolution, helping bacteria adapt to living in a sputum-like environment.'

Davies EV, James CE, Williams D et al (2016) Temperate phages both mediate and drive adaptive evolution in pathogen biofilms. *Proc Natl Acad Sci U S A* pii: 201520056

## Shingles is a persistent risk factor for stroke

Researchers from the Department of Neurology at the University of Ulsan College of Medicine in Seoul showed that herpes zoster infection not only raised the risk of ischaemic and haemorrhagic stroke but also that of a transient ischaemic attack (doi: 10.1016/j.cmi.2016.03.003).

They used a large South Korean health database of more than 1 million people to examine the relationship between herpes zoster infection and transient ischaemic attack or stroke. The prospective cohort study followed up 766 179 adults for 11 years from 2003.

## Liver diseases have differing patterns in ethnic minorities in US

Little is known about how chronic liver disease and cirrhosis affect ethnic minority populations in the USA. Researchers found that the prevalence of chronic liver disease ranged from 3.9% in African Americans and native Hawaiians to 4.1% in whites, 6.7% in Latinos and 6.9% in Japanese (Setiawan et al, 2016).

Non-alcoholic fatty liver disease was the most common cause of chronic liver disease in all ethnic groups combined (52%), followed by alcoholic liver disease (21%).

Non-alcoholic fatty liver disease was the most common cause of cirrhosis in the entire study, and by ethnicity, it was also the most common cause of cirrhosis in Japanese Americans, native Hawaiians, and Latinos, accounting for 32% of cases. Alcoholic liver disease was the most common cause of cirrhosis in whites (38.2%), while hepatitis C virus was the most common cause in African Americans (29.8%).

Setiawan VW, Stram DO, Porcel J, Lu SC, Le Marchand L, Nouredin M (2016) Prevalence of chronic liver disease and cirrhosis by underlying cause in understudied ethnic groups: The Multiethnic Cohort. *Hepatology* (doi: 10.1002/hep.28677)