

Clinical features and prognostic factors of listeriosis

A national prospective observational cohort study was carried out in France to characterize the clinical features and prognostic factors of listeriosis, a severe foodborne infection and a notifiable disease (Charlier et al, 2017).

The authors enrolled 818 cases from 372 centres, including 107 maternal–neonatal infections, 427 cases of bacteraemia and 252 cases of neurolisteriosis. Only five (5%) of 107 pregnant women had an uneventful outcome. Of 107 mothers 26 (24%) experienced fetal loss, but never after 29 weeks of gestation or beyond 2 days of admission to hospital.

In 212 (84%) of 252 patients neurolisteriosis presented as meningo-encephalitis; brainstem involvement was only reported in 42 (17%) of 252 patients. Three-month mortality was higher for bacteraemia than neurolisteriosis. Survival was significantly reduced in patients with neurolisteriosis treated with adjunctive dexamethasone.

The study found the severity of listeriosis to be higher than reported elsewhere, and also determined the time window for fetal losses.

Charlier C, Perrodeau E, Leclercq A et al, on behalf of the MONALISA study group (2017) Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. *Lancet Infect Dis* 17(5): 510–519. [https://doi.org/10.1016/S1473-3099\(16\)30521-7](https://doi.org/10.1016/S1473-3099(16)30521-7)

Resource for families of babies expected to have very short lives

Charity Together for Short Lives has launched its Perinatal Pathway for Babies with Palliative Care Needs to support professionals to help families with seriously ill babies have more choice in their child's care, no matter how short the child's life may be. Developed with expert input from ethicists and clinicians working across obstetrics, antenatal and neonatal care, and children's palliative care, the pathway can be downloaded for free from www.togetherforshortlives.org.uk/perinatalpathway

Non-invasive post-mortem has the potential to replace invasive autopsy

A breakthrough in how autopsy practice is conducted in the UK and around the world could be possible following the results of a new study (Rutty et al, 2017).

England and Wales have one of the highest frequencies of autopsy in the world. Implementation of post-mortem computed tomography, enhanced with targeted coronary angiography, in adults to avoid invasive autopsy would have cultural, religious and potential economic benefits. Previously the lack of circulation in the cadaver has prevented the use of contrast agents. This has been overcome by developing a novel minimally invasive coronary artery angiography technique. A number of these techniques have been developed over the last few years, but this is the first large-scale fully autopsy-controlled trial to demonstrate their efficacy in adult natural death.

The single-centre, prospective, controlled study assessed the diagnostic accuracy of post-mortem coronary angiography as a first-line technique in post-mortem investigations. The study selected cases of natural and non-suspicious unnatural death referred to Her Majesty's (HM) Coroners.

Professor Guy Rutty, East Midlands Forensic Pathology Unit, Leicester Royal Infirmary, Leicester, explained: 'We developed a quick and minimally invasive approach to improve diagnostic accuracy. This uniquely uses a combination of standard contrast

agent (positive) and air (negative) to show the coronary artery lumens and ventricular cavities.'

The team applied the post-mortem coronary angiography technique to a cohort of 240 deaths investigated by the HM Coroner. A cause of death could be given in 92% of cases, based on 'the balance of probabilities', the burden of proof required by the HM Coroner. Comparison with independently generated autopsy results showed that post-mortem coronary angiography had a similar accuracy to autopsy, did not miss autopsy-identifiable unnatural or 'reportable' causes of death, and would also not significantly change population 'cause of death' statistics.

Co-author Professor Bruno Morgan, from the Radiology Department, Leicester Royal Infirmary, Leicester, added: 'Post-mortem computed tomography enhanced by targeted coronary angiography can diagnose the cause of death in up to 90% of HM Coroner investigations for suspected natural death. This is the most successful application of post-mortem computed tomography and post-mortem coronary angiography to date in natural death, and shows that a significant number of deaths could be investigated without the need for an invasive autopsy.'

Post-mortem coronary angiography was found to be superior at identifying trauma and haemorrhage, whereas autopsy was superior at identifying pulmonary thromboembolism. Both tests had different strengths and weaknesses in heart and lung disease.

Professor Rutty cautioned: 'Both autopsy and post-mortem coronary angiography have different strengths and weaknesses as investigative approaches. When a higher burden of proof is required the "gold standard" of death investigation should include both post-mortem computed tomography and invasive autopsy.'

The findings are unique from an international perspective as they focus on natural death. A small number of unnatural deaths were also examined, showing post-mortem coronary angiography was also useful in these cases.

Professor Guy Rutty, University of Leicester, East Midlands Forensic Pathology Unit, Leicester Royal Infirmary, Leicester



Rutty GN, Morgan B, Robinson C et al (2017) Diagnostic accuracy of post-mortem CT with targeted coronary angiography versus autopsy for coroner-requested post-mortem investigations: a prospective, masked, comparison study. *Lancet* [https://doi.org/10.1016/S0140-6736\(17\)30333-1](https://doi.org/10.1016/S0140-6736(17)30333-1)

Low adoption of recommendations to reduce radiation exposure during nuclear cardiology

A study in 65 countries has revealed low adoption of International Atomic Energy Agency (IAEA) recommendations to reduce radiation exposure during nuclear cardiology procedures (Hulten et al, 2017).

The IAEA developed eight quality metrics for responsible radiation use in nuclear cardiology: avoiding thallium-201 stress testing, avoiding dual isotope testing, avoiding too much technetium-99m and thallium-201, using stress-only imaging, use of camera technologies to reduce dose, use of weight-based dosing strategies for technetium-99m, and avoiding inappropriate dosing that can lead to 'shine-through' artefacts. A goal of 9 mSv or less radiation exposure per scan has been recommended.

The IAEA Nuclear Cardiology Protocols Study (INCAPS) assessed adherence to the eight quality metrics during 1 week in 2013, studying 308 nuclear cardiology laboratories in 65 countries. The survey included 7911 nuclear cardiology scans. There was significant variability in adherence to the quality metrics across laboratories and regions. There was low adherence overall, with most sites implementing fewer than half of the quality metrics.

When the researchers performed multivariable logistic regression analysis, they found that the practices most strongly associated with achieving a 9 mSv or less scan

were the use of stress or rest only imaging, avoiding thallium, and use of camera technologies to reduce radiation dose.

Dr Edward Hulten, a cardiologist at the Walter Reed National Military Medical Center, Bethesda, USA said: 'When the 9 mSv recommendation was made in 2010 it was suggested that it should be achieved in 50% of scans by 2014. The INCAPS survey shows that there is still work to do. It is possible to reduce radiation exposure with existing techniques. Cadmium zinc telluride cameras are more sensitive and allow for reduced dose scanning. With certain tracers you can achieve 1 mSv or less. But some scans use more than 30 mSv, so there is huge variability.'

Dr Hulten concluded: 'The INCAPS survey is a crucial step towards improving patient care in the field of nuclear cardiology by quantifying worldwide adherence to best practices. Any test involving ionizing radiation will increase cancers within a population but the risk must be weighed against the benefit of gaining information about heart disease. The 9 mSv goal is achievable, and the lower the better.'

Hulten E, Mercuri M, Pascual TN et al (2017) Odds of less than 9 mSv myocardial perfusion study in association with camera technology, reconstruction software, and acquisition protocols: from the IAEA nuclear cardiology protocols study (INCAPS). Abstract P362. *Eur Heart J Suppl* 18(Suppl 1): i82

Rise in emergency hospital admissions for young children

A new study from the Nuffield Trust and Health Foundation has found that the number of babies and young children admitted to hospital in an emergency has risen by almost a third over the past decade (Keeble and Kossarova, 2017). Many children are being admitted to hospital for conditions like asthma and tonsillitis – admissions that could potentially have been avoided with better care and support out of hospital.

The study draws on in-depth analysis of hundreds of thousands of patient records to explore how children and young people have been accessing emergency hospital care from 2006/7 to 2015/16. Babies (under 1 year

old) and children under 4 years of age experienced the biggest rise in admissions, with the numbers of emergency admissions growing by 30% and 28% respectively between 2006/7 and 2015/16.

Keeble E, Kossarova L (2017) Focus on: Emergency hospital care for children and young people. What has changed in the past 10 years? www.qualitywatch.org.uk/sites/files/qualitywatch/field/field_document/QualityWatch%20CYP%20report.pdf (accessed 24 May 2017)



Additional vitamin D only strengthens bone in those with significant deficiency

An international study of older adults, presented at the 44th European Calcified Tissue Society Congress, Salzburg, Austria, has found that untargeted provision of vitamin D supplements has little clinical benefit in preventing osteoporosis. Future trials should focus on older adults who have baseline vitamin D levels ≤ 30 nmol/litre.

Projections for future palliative care needs

A study has estimated future population palliative care need in England and Wales (<https://doi.org/10.1186/s12916-017-0860-2>). By 2040, annual deaths in are projected to rise by 25.4%. If age- and sex-specific proportions with palliative care needs remain the same as in 2014, the number of people requiring palliative care will grow by 25.0%.

Socioeconomic and racial disparities in lupus

Two new American studies have uncovered socioeconomic disparities related to the health of patients with lupus. The first found a link between poverty and worse disease-associated medical complications over time (<http://doi.wiley.com/10.1002/art.40134>), and the second discovered that the frequency of adverse pregnancy outcomes in black and Hispanic patients with lupus is higher than that in white women with the disease (<http://doi.wiley.com/10.1002/acr.23263>).

Nearly one-quarter of patients say mechanical heart valve disturbs their sleep

Research presented at EuroHeartCare 2017 investigated how the noise of a mechanical heart valve affected patients' lives, in particular their sleep, and whether there were any differences between women and men.

In April 2013 all 1045 patients who had undergone aortic valve replacement at Haukeland University Hospital, Bergen, Norway between 2000 and 2011 were invited to participate in a postal survey. Of the 908 who responded, 245 had received a mechanical valve and were included in the analysis.

Patients were asked about the sounds the valve made. They ranked the noise on a scale of 0 (does not disturb them at all) to 10 (causes maximum stress). The Minimal Insomnia Symptom Scale was used to give patients a score of 0 to 12 for insomnia.

Patients were 60 years old on average and 76% were men. Nearly one-quarter (23%) said the valve sound disturbed them during sleep and 9% said it disturbed them during the day.

A total of 87% of men and 75% of women reported that they were able to hear the closing sound of their mechanical valve. Women were more disturbed by the valve sound than men.

Is there a prodromal period in multiple sclerosis?

A matched cohort study examined patterns of health-care use before a first demyelinating event to establish whether a multiple sclerosis prodromal period exists (Wijnands et al, 2017).

Data from linked health administrative and clinical databases from four Canadian provinces were used to compare hospital, physician and prescription use data from people with multiple sclerosis and matched general population controls in the 5 years before the first demyelinating disease claim or clinically reported symptom onset. The health administrative cohort included 14 428 multiple sclerosis cases and 72 059 matched controls for whom data were available between April 1984 and April 2014. The primary outcome was all-cause use of health care during each of the 5 years before the health administrative or clinical index date.

Annual health-care use increased steadily between 5 years and 1 year before the first demyelinating disease claim in people with multiple sclerosis compared with controls, being statistically significant for hospital admissions, physician claims and prescriptions, suggesting the existence of a measurable multiple sclerosis prodrome.



Professor Helen Tremlett, Faculty of Medicine (Neurology), UBC Hospital, University of British Columbia Vancouver, Canada

Commenting on the findings, Professor Helen Tremlett, UBC Hospital, University of British Columbia Vancouver, Canada, said: 'Multiple sclerosis is the leading cause of neurological disability in young adults aside from physical trauma. By identifying a measurable prodromal period in multiple sclerosis, our study suggests that there is potential to recognize and possibly diagnose multiple sclerosis earlier, thereby extending the window during which people

could be treated.

She highlighted: 'In addition, our findings have major implications when searching for the cause of multiple sclerosis. By identifying a prodrome, this work helps to determine the causally (ir)relevant time period in which to identify factors that might trigger the onset of multiple sclerosis.'

These findings have clinical and research implications, including the establishment of an earlier window of opportunity to identify and potentially treat multiple sclerosis.

Wijnands JMA, Kingwell E, Zhu F et al (2017) Health-care use before a first demyelinating event suggestive of a multiple sclerosis prodrome: a matched cohort study. *Lancet Neurol* 16(6): 445–451. [https://doi.org/10.1016/S1474-4422\(17\)30076-5](https://doi.org/10.1016/S1474-4422(17)30076-5)

Making 'best interests' decisions in paediatric intensive care

A qualitative study has looked at how parents and clinicians make life or death medical decisions involving very young children (Birchley et al, 2017). The findings may offer insight into how the 'best interests' of a child are decided when parents and clinicians cannot reach a consensus.

The research discussed these issues with parents and clinicians who had gone through difficult situations in which they had tried to agree on best interests of very sick children. A total of 39 interviews took place with parents of children who had been patients on paediatric intensive care units, doctors and nurses working on paediatric intensive care units, and members of

clinical ethics advisory committees. The study focused on decisions about children who do not take part in decision making because they are too young, too sick or have a pre-existing disability.

The study found that parents and clinicians viewed children's interests differently in decision making. Doctors and nurses tended to think that parental interests sometimes carried more weight than those of the child. When a decision about treatment needed to be made, doctors encouraged parents to consider medical opinion. Sometimes parents could not agree with their doctor until their child began to show physical signs of decline in their condition.

Lead author Dr Giles Birchley, from the Centre for Ethics in Medicine, University of Bristol, Bristol, commented: 'While disagreements in end-of-life decisions are rare, there is considerable reluctance to use the courts as the decision makers of last resort.

He emphasized: 'While this study recommends that the way decisions are made could be changed, more research is needed to respond to the complexity of decision making in such cases.'

Birchley G, Gooberman-Hill R, Deans Z, Fraser J, Huxtable R (2017) 'Best interests' in paediatric intensive care: an empirical ethics study. *Arch Dis Child* <https://doi.org/10.1136/archdischild-2016-312076>

Standardized assessment evaluates medical students' competence at prescribing medications

A standardized assessment ensures that students who graduate from UK medical schools have achieved a minimum standard of knowledge and skill related to prescribing medications (Maxwell et al, 2017).

Professor Simon Maxwell, of the University of Edinburgh and colleagues from the British Pharmacological Society and Medical Schools Council created a national assessment that would identify graduates who need more training and supervision in prescribing, and in the future might also highlight which training methods are most successful in developing competent practitioners.

Over 5 years, the investigators developed the Prescribing Safety Assessment as a 2-hour online assessment of competence. The online delivery system and unique approach to automated online marking of large numbers of prescriptions allowed them to overcome the practical difficulties of assessing prescribing.

The Prescribing Safety Assessment was taken by 7343 final-year medical students in 31 UK medical schools. The overall pass rate



Professor Simon Maxwell, Clinical Pharmacology Unit, Edinburgh Medical School, University of Edinburgh, Edinburgh

was 95% with rates for individual papers ranging from 93 to 97%. The assessment was re-taken by 261 students who had failed, and 80% of those candidates passed. There was significant variation in performance between students from different medical schools.

'We believe that this is the first example of a large-scale nationally applied assessment of prescribing competence anywhere in the world,' said Professor Maxwell.

'We have now participation by medical schools in Ireland and Malta, with growing interest about building on this assessment from educators in Australia, New Zealand, Canada and India. Also, in the UK, we are exploring whether the Prescribing Safety Assessment and its associated training modules might have utility as an assessment for more senior doctors and pharmacists.'

Maxwell SRJ, Coleman JJ, Bollington L, Taylor C, Webb DJ (2017) Prescribing Safety Assessment 2016: Delivery of a national prescribing assessment to 7,343 UK final-year medical students. *Br J Clin Pharmacol* <https://doi.org/10.1111/bcp.13319>

Combining heroin and pregabalin or gabapentin linked to significant rise in deaths from overdose



Professor Matthew Hickman, Professor of Public Health and Epidemiology, School of Social and Community Medicine, University of Bristol, Bristol

The increase in prescriptions for pregabalin and gabapentin, used widely to treat a range of neurological disorders, is closely correlated with a rise in the number of overdose deaths in England and Wales (Lyndon et al, 2017).

Prescriptions for pregabalin and gabapentin increased from 1 million in 2004 to 10.5 million in 2015 (i.e. a 24% increase year on year) and concern has arisen about their diversion and misuse. The number of deaths in England and Wales

involving gabapentoids increased from fewer than one per year before 2009 to 137 in 2015, of which 79% also involved opioids such as heroin. Interviews with heroin users reported that taking pregabalin and gabapentin was associated with a feeling of loss of control and an enhanced effect of heroin.

Professor Matthew Hickman, Professor of Public Health and Epidemiology in the School of Social and Community Medicine, University of Bristol, and co-author of the study, said: 'The number of overdose deaths involving the combination of opioids with gabapentin or pregabalin has increased substantially and there is evidence now that their concomitant use... increases the risk of acute overdose deaths.'

Lyndon A, Audrey S, Wells C et al (2017) Risk to heroin users of polydrug use of pregabalin or gabapentin. *Addiction* <https://doi.org/10.1111/add.13843>

Cervical cancer survivors frequently suffer from long-term fatigue, insomnia and hot flashes

Around half of women who have been treated for locally advanced cervical cancer suffer from symptoms of insomnia, fatigue or hot flashes at some point according to findings from the prospective, observational, multicentre EMBRACE study (Smet et al, 2017).

The study involved 1176 patients with locally advanced cervical cancer, treated at 22 centres worldwide between 2008 and 2015. All received the gold-standard treatment of radiotherapy combined with chemotherapy, followed by brachytherapy. Patients were followed up for an average of 27 months.

The results show that 64% of women were experiencing fatigue to some degree at least once during their regular follow-up examinations in the years after treatment. For insomnia, the figure was 43% and for hot flashes it was 50%.

Dr Stéphanie Smet, a resident in radiation oncology at the Medical University of Vienna, Austria, who presented the research, told the European Society for Radiotherapy and Oncology congress: 'Our study shows that around half of women with locally advanced cervical cancer are, at some point, suffering from mild to moderate fatigue, insomnia and hot flashes. These symptoms could have a serious impact on patients' daily life, possibly influencing how they feel in their professional, social and family life.'

She continued: 'More and more women diagnosed with this type of cancer are surviving for longer, thanks to advances in radiotherapy. This is a relatively young group of patients, so many will possibly face decades of coping with their symptoms.'

Smet AS, Najjari-Jamal D, Jensen NBK et al (2017) Fatigue, insomnia, hot flashes (CTCAE) after definitive RCHT+IGABT for cervical cancer (EMBRACE). Abstract no OC-0051. *Radiother Oncol* 123(Suppl 1): S22