

Haunted castles and exploding lungs

THE pig lung appeared determinedly still. Glistening pinkly, it hung innocently from its apparatus. Yet no other source could explain the disturbing “breathing” sounds audible half way across the conference hall.

Leaning closer, I studied the organ suspiciously. A small, blue cyst was visible near the proximal aspect of one lobe, but otherwise all seemed normal. Then, with a gasping intake of “breath”, the lung suddenly inflated.

Misinterpreting my fascinated horror as enthusiasm, a technician leapt forward keenly. The lung, he explained, was sourced from a slaughterhouse, and could be used to investigate mechanical factors determining toxin inhalation,

thereby sparing laboratory animals. By altering flow rates and pressures, “breathing” patterns could be varied.

Enclosed by clear, reinforced perspex, the lung could even be used for endoscopic surgical training. Why, exactly, the perspex needed to be reinforced, I dared not inquire, as the breathing became frighteningly rapid...

The lung was on display in September at the 15th Congress on Alternatives to Animal Testing, at the Johannes Kepler University, in Linz, Austria.

Based on conservative estimates, around 127 million non-human vertebrates worldwide are used within biomedical research, toxicity testing or education, and such use is increasing¹. Yet the limitations incurred through modelling humans by animals are increasingly recognised.

Unrealistic doses

These include differences between species and genders – with subsequent effects on toxic- and pharmacokinetics (bodily distribution), or pharmacodynamics (mechanisms of action, and drug effects).

They commonly include unrealistic doses and exposure durations; loss of biological variability or predictivity, resulting from in-bred strains, young animals, restriction to single genders, and inadequate group sizes; lack of co-

morbidities or other human risk factors; and stress-related physiological or immunological distortions^{2,4}.

Unsurprisingly, the human utility of animal models has been increasingly questioned. Of 20 published systematic reviews located during a recent, comprehensive search, animal models demonstrated significant potential to contribute toward the development of human clinical interventions in only two cases, one of which was contentious.

Seven additional reviews failed to demonstrate utility in reliably predicting human toxicological outcomes, such as carcinogenicity and teratogenicity. Results in animal models were frequently equivocal, or

inconsistent with human outcomes⁵.

However, a broad range of investigative tools exists, with potential to decrease or replace laboratory animal use⁶. These include computerised modelling, minimally-sentient animals from lower phylogenetic orders, and a variety of tissue cultures, including immortalised cell lines, embryonic and adult stem cells, and organotypic cultures.

Human cell culture assays

Bacterial, yeast, protozoal, mammalian or human cell culture assays exist for a wide range of toxic and other endpoints. These may be static or perfused, and may be used individually, or combined within test batteries. Human hepatocyte cultures and metabolic activation systems offer potential assessment of metabolite activity, and organ-organ interaction.

Micro-array technology (“gene chips”) allow genetic expression profiling, increasing the speed of toxin detection, well prior to more invasive endpoints.

Enhanced human clinical trials utilising microdosing, staggered dosing, and more representative study populations and durations, as well as surrogate human tissues, advanced imaging modalities and human epidemiological, sociological and psychological studies, may increase understanding of illness aetiology and pathogenesis, and facilitate the development of safe and effective pharmacologic interventions.

Non-animal models cannot, of course, answer all questions about

humans, particularly given present technological limitations.

However, the same is certainly true of animal models, which have less capacity for further development. And, particularly when human tissues are used, alternative models may generate faster, cheaper results, more reliably predictive for humans, whilst yielding greater insights into human biochemical processes.

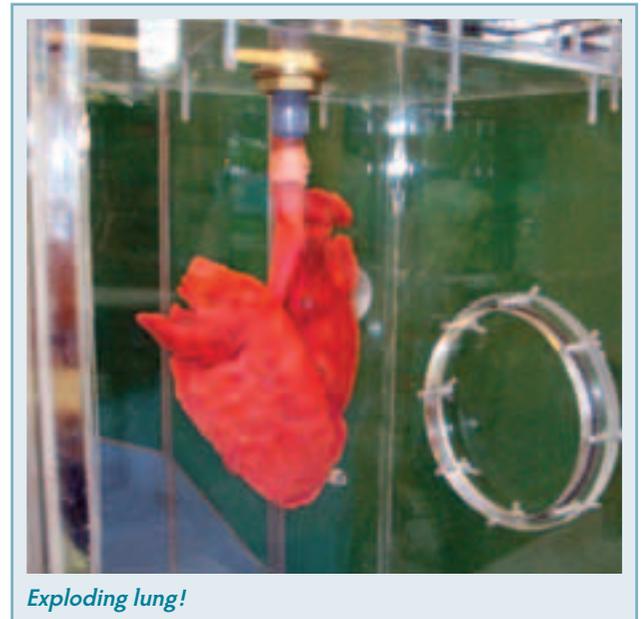
National legislation frequently requires consideration of alternatives to laboratory animal use. Researcher compliance, however, may be disturbingly poor.

Non-compliance

A 2000 survey identified a range of common areas of non-compliance of US researchers with regulations of the Animal Welfare Act. The most common was inadequate consideration of alternatives – at 600-800 research facilities.

Even veterinary associations appear uncritical in their support for animal experimentation, as indicated by a recent survey of the positions of the World Veterinary Association and four national veterinary associations, including the British Veterinary Association⁷.

Accordingly, mechanisms to increase awareness and use of non-animal alternatives are clearly



Exploding lung!

warranted. Considerably more stringent compliance with legislation requiring their use could – and should – become a prerequisite of research funding, experimental licensing, and publication of results.

Despite my best efforts, the persistent heavy breathing sounds were impeding my ability to concentrate on my colleagues’ impressive posters and displays. It was time to seek some fresh air. The rolling hills surrounding the Danube River town of Linz were covered by deep, shadowed forests, broken by the occasional picturesque chalet, nestled beside a field, and the odd graveyard overgrown by flowers.

Battlements spotted

Close to dusk on the final day, I was thrilled to spy battlements across a valley. Hailing from a country without any, I get rather excited by mediaeval ruins. A suitably sinister castle soon loomed out of the deepening gloom, and it occurred to me, as a bat launched itself from a tower, that we did have one similar structure in Western Australia.

Perched on a cliff overlooking the bay in which their prison ships were anchored, the Roundhouse jail was built by my convict ancestors under armed guard, to house them. It was the first building in our state.

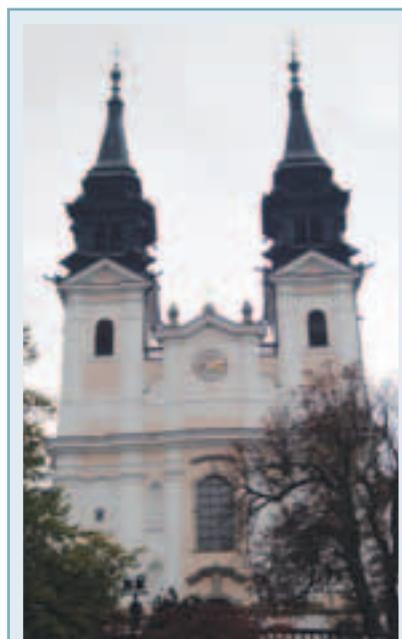
As shadows lengthened beyond the heavy iron-bound castle door, mysteriously opened by some unseen hand, I recalled that some believe the unquiet spirits of my ancestors dwell there still. I wondered whether I might not meet similar apparitions within the grim stone walls of this faraway land, and whether the shades of stray tourists would count among their number...

Such unanswered questions, at least, remained to haunt me, as I reluctantly turned toward the airport



ANDREW KNIGHT continues his series on CPD with a difference with a report on his recent trip to Austria

London-based veterinarian Andrew Knight is the president of Animals Count, a political party for people and animals (www.AnimalsCount.org).



Haunted castle...



At the Vets Now congress last month – Dr Richard Dixon (centre), the founder and group managing director of Vets Now, with Glen Gribbon, who joined in September as MD of Vets Now Emergency (he was recently named Scottish Marketer of the Year) and Amanda Boag, the clinical director. Right: two of the stands in the exhibition – Pet Blood Bank UK and JAK Marketing.



Emergency and critical care congress now well-established

It is a measure of how rapidly the interest in emergency and critical care work is growing in the UK that last month's fifth congress run by Vets Now was almost too big for the venue – the Majestic Hotel in Harrogate.

Many of the well-over 500 delegates had to be accommodated in

other hotels and the function rooms were packed for many of the events. A substantial number of delegates were from "normal" practices and vets outnumbered nurses by two to one.

Vets Now set up its first clinic to provide out-of-hours emergency care in 2001, in Glasgow, and now has 33 centres across the UK employing a total of more than 330 clinical staff. It hopes, says group MD Dr Richard Dixon, to double the number of clinics during the next five years.

"It's a rewarding arena for vets," he told a small press conference at the congress. "They see the more interesting cases and it changes their perspective on their career. Our staff are a special group of people, passionate and committed, and we want them to make a difference."

To this end, the group presents

LOOKING AHEAD

European congress – The 8th European Veterinary Emergency and Critical Care Congress is to be held in Berlin from 12th to 14th June. The programme will cover fluid therapy, transfusion, monitoring, complications, urinary infections and nutrition. Among the speakers will be Amanda Boag of Vets Now. For details see www.eveccs2009.org or e-mail eveccs@gmail.com.

International congress – the 15th International Veterinary Emergency and Critical Care Symposium will be held in Chicago from 9th to 13th September. Details on www.veccs.org or e-mail info@veccs.org.

UK congress – the 6th Emergency & Critical Care Vets Now annual congress will be in Harrogate on 12th and 13th November 2009. Details will be available in due course on www.vets-now.com.

and my impending flight to London. Despite the eminent suitability in décor – if not age – of certain of my locum placements, such paranormal experiences have been sadly lacking in my veterinary world, to date. I must return someday, I thought, with a very large torch!

References

1. Knight, A. (2008) 127 million non-human vertebrates used worldwide for scientific purposes in 2005. *ATLA*: in press.
2. Hartung, T. (2008) Food for thought ... on animal tests. *ALTEX* 25 (1): 3-9.
3. Hartung, T. (2008) Thoughts on limitations of animal models. *Parkinsonism Relat. Disord.*: in press.
4. Matthews, R. A. (2008) Medical progress depends on animal models – doesn't it? *J. R. Soc. Med.* 101: 95-98.
5. Knight, A. (2007) Systematic reviews of animal experiments demonstrate poor human clinical and toxicological utility. *ATLA* 35 (6): 641-659.
6. Knight, A. (2008) Non-animal methodologies within biomedical research and toxicity testing. *ALTEX* 25 (3): 213-231.
7. De Boo, J. and Knight, A. (2006) Educating the veterinary professional about animal welfare. *ALTEX* 23 (spl. issue: Proceedings: 5th World Congress 2005): 71-74.

MAD (for make a difference) awards at each year's congress "to celebrate individual dedication and achievement". The Bradford Clinic was named "Team of Stars"; other awards went to Natasha Melbourne from Belfast (Star Veterinary Surgeon), Donna Johnson of Bradford (Star Veterinary Nurse), Anita Kerfoot of Stoke (Star Receptionist), Gareth Roscoe of Winchester (Ambulance Star) and Lisa Docherty of Dunfermline (Support Office Star).

Speakers from the UK and abroad

covered topics ranging from spinal trauma to charging for professional time, care of the GDV patient to reading ECGs, fluid therapy to the management of seizures.

There was also a "stream" in which people presented 10-minute case studies, which included, for example, an adder bite in a dog (Albert Schuen), snail bait toxicity (Rene Mostert), severe acute pancreatitis (Glen McIntosh) and the retching dog (Joe Leathers).

■ Further report next month.

Right: there was plenty of activity on the social side including a casino evening after the gala dinner. Below: Idexx had a stand featuring plenty of high-tech laboratory equipment and also took groups of delegates to workshops at its Wetherby premises.

