Feature Articles

Could we have safer medicines through non-animal testing?

The use of animals in medical research is an emotionally charged topic, but the scientific rationale behind their use is rarely questioned. Margaret Clotworthy describes an initiative doing just that.

A groundbreaking conference last November brought together eleven scientists from around the world who specialise in developing drug safety test methods that focus on human biology. The conference, 'Speed and Safety in Drug Discovery', was held at the Royal Society in London and was hosted by Safer Medicines Trust. This charity is concerned with the use of animals in medical research, but it differs from the others in that the Trust's concern is for the patients who ultimately receive the drugs, rather than the animals. We believe that using animals is actually ineffective at testing the safety of new medicines. It not only fails to stop harmful drugs from reaching people, it also prevents treatments that would be safe and effective from reaching patients who need them.

The clinical trial at Northwick Park hospital in March 2006, where six previously healthy young men were rushed to intensive care with multiple organ failure, put a spotlight on safety issues surrounding clinical trials. The drug had already been tried out on monkeys at 500 times the dose the men received, yet this was not sufficient to reveal its dangers¹. Although it was exceptional for all the volunteers to suffer such severe reactions, the fact is that nine out of every ten new drugs fail in clinical trials after success in animal tests². Even the drugs that succeed in clinical trials and reach the market are not safe for everyone: side effects are a leading killer in the western world, after cancer, heart disease and stroke^{3,4,5}. Moreover, adverse reactions to prescription drugs are now estimated to cause one million hospital admissions per year at a cost to the NHS of £2 billion⁶. Safer Medicines Trust does not claim that an over-reliance on animal testing is solely responsible for these statistics; but could better pre-human testing improve the situation?

Science has come a long way since the UK Medicines Act, introduced in 1968 in the wake of the thalidomide tragedy, made animal testing of new drugs mandatory. Extensive animal testing had in fact shown thalidomide to be perfectly safe⁷, and it was prescribed to pregnant women to treat their morning sickness, causing thousands of babies worldwide to be born with deformed limbs in the 1950s and early 1960s. However, the testing technologies then available were very limited compared with those at our disposal today, and what was clear from the astonishing range of presentations at the November conference is that we may no longer need to depend on the unreliable indications from animals at all.

Experts in human tissue science spoke of the array of tests that can now be conducted using tissue sourced ethically from surgery, for example, or using cells grown indefinitely in the lab. American company Hurel – their name deriving from 'Human Relevant' – uses interconnected human tissue samples to represent a 'whole body on a chip'. A particularly exciting technique developed by another US company, VaxDesign, involves growing up miniature immune systems for vaccine testing from donated blood samples – something undreamed of even a few years ago.

The use of computer models to predict which drugs would be toxic, and to make dosing safer, was also discussed, before the conference moved on to how to take drugs into humans safely for the first time. One option is microdosing, which uses miniscule doses of new drugs, combined with ultrasensitive imaging and analysis equipment, to reveal how the drugs are metabolised in humans safely and with unsurpassed accuracy – enabling safer clinical trials. The motto of Xceleron, the world's first microdosing company, is that "the best model for human drug development is human beings" – a sentiment that was echoed many times throughout the event.

Finally, an expert from the University of Vienna explained microdialysis, which uses very sensitive probes to detect what is happening in a tissue or to a drug in a highly localised part of the body. This is already used extensively in Sweden to monitor the brains of patients suffering from severe brain injuries.

Safer Medicines Trust believes it is time to put animal tests to the test against these amazing new technologies, which could deliver medicines to patients not only more safely but much more quickly and cheaply as well. We will shortly be launching an initiative to put pressure on the government to do just that. Details of how you can help will be available at our website, http://www.safermedicines.org/

Dr Margaret Clotworthy is Science Consultant to Safer Medicines Trust, a registered charity whose goal is to protect human health by promoting human-specific medical research.



References

1. Stebbings R, Findlay L, Edwards C, Eastwood D, Bird C, North D, Mistry Y, Dilger P, Liefooghe E, Cludts I, Fox B, Tarrant G, Robinson J, Meager T, Dolman C, Thorpe SJ, Bristow A,

Wadhwa M, Thorpe R, Poole S (2007). "Cytokine Storm" in the phase I trial of monoclonal antibody TGN1412: better understanding the causes to improve preclinical testing of immunotherapeutics. The Journal of Immunology, 179(5) 3325-3331.

2. US Food and Drug Administration (FDA) (2004). Innovation or Stagnation: challenge and opportunity on the critical path to new medical products. http://www.fda.gov/

 Lazarou J, Pomeranz BH, Corey PN (1998). Incidence of adverse drug reactions in hospitalized patients. Journal of the American Medical Association, 279: 1200-1205.

4. Lasser KE, Allen PD, Woolhandler SJ, Himmestein DU, Wolfe SM, Bor DH (2002). Timing of new black box warnings and withdrawals for prescription medications. Journal of the American Medical Association, 287: 2215-2220.

 5. EUobserver (2008). Adverse reactions to medication is the fifth most common cause of death in hospitals according to the European Commission. http://euobserver.com/9/26973.
6. Boseley S (2008). Adverse drug reactions cost NHS £2bn. The Guardian. 3 April

7. Knobloch J, Reimann K, Klotz L O, Rüther U (2008). Thalidomide resistance is based on the capacity of the glutathione-dependent antioxidant defense. Molecular Pharmaceutics (online), October 22. http://pubs.acs.org/journal/mpohbp

17