Dr Hadwen Trust

Replacing Animals in Medical Research

The Dr Hadwen Trust is the UK's leading medical research charity funding and promoting exclusively non-animal techniques to replace animal experiments. Our work benefits people whilst also saving laboratory animals.

Computer simulations

A 1995 grant from the Dr Hadwen Trust assisted the development of computer models of human reproductive pathophysiology.

Based on human studies - clinical, *in vitro* and *ex vivo* - the models avoided experiments on sheep, whose fetoplacental physiology differs markedly from that of humans.

First, the simulations explained the diagnostic change in uterine artery blood flow in pregnant women at risk of pre-eclampsia. The cause was pinpointed as an abnormality in artery wall elasticity, overturning the previous hypothesis (1).

Further modelling explained how certain vascular connections in the placenta cause twin-twin transfusion syndrome, an often fatal condition for identical twin fetuses. This allowed the development of a clinical test to predict women's susceptibility to the syndrome and enabled the severity of the condition to be assessed, so that the optimal treatment is selected (2).

The computer models continue to be improved, yielding important insights (3). With added physiological features, the newest models will help determine the efficacy of new therapies (4).

1. Talbert DG (1995). Ultrasound Obstet. Gynecol. 6:261-271.
2. Tan TYT et al (2004). Obstet. Gynecol. 103:1174-1180.
3. Denbow ML et al (2006). Prenat. Diagn. 26:433-442.
4. van den Wijngaard JPHM et al (2005). Am. J. Physiol. Regul. Integr. Comp. Physiol. 288:R799-R814.

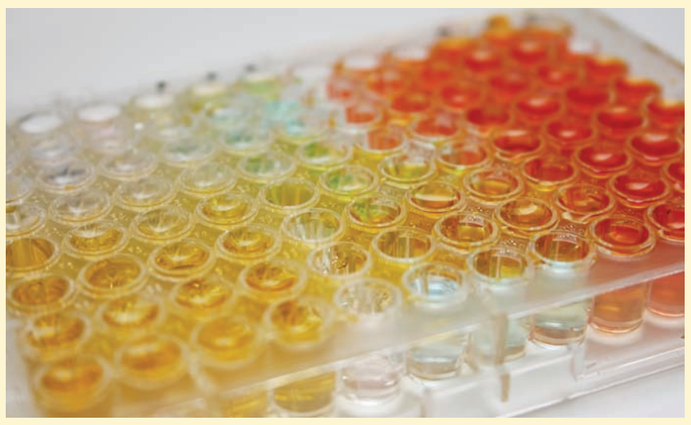
'Fingerprinting' pathogens

A Dr Hadwen Trust grant in 2000 led to the development of mass spectral patterns to identify bacterial strains, as a replacement for animal bioassays.

Matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry **(MALDI-TOF-MS)** produces a mass spectral profile of the ionisable components of cell surfaces. These profiles, combined with new techniques of protein and DNA analysis, have proved reliable for identifying various bacterial species and strains.

A study of 18 strains of *Peptostreptococcus micros* demonstrated unequivocally that MALDI-TOF-MS could distinguish between virulent and avirulent types. Previously, the only reliable test required guinea pig inoculation, the virulent form producing an abscess on the animal's back or leg.

Two similar species of *Shigella* (which causes dysentery), previously only differentiated by serology using animals, were also largely distinguishable using MALDI-TOF-MS. Other studies were carried out to delineate the serotypes of human pathogens and a standard method established (5).



MALDI-TOF-MS analysis is simple, fast and cost-effective and is providing better methods for disease control (6). The Health Protection Agency uses fewer animals as a result.

5. Shah HN et al (2002). Clin. Infect. Dis. 35:S58-S64.
6. Shah HN et al (2006). Surface enhanced laser desorption/Ionization time of flight mass spectrometry (SELDI-TOF-MS): a potentially powerful tool for rapid characterisation of microorganisms. In: Encyclopaedia of Rapid Microbiological Methods, vol. 3. MJ Miller (ed). Publ. DHI Publishing, USA.

Volunteers in brain research

The Dr Hadwen Trust has helped to pioneer novel imaging and related techniques which, applied to volunteers, have replaced experiments on animals, notably primates.

Animal experiments with intracellular or field electrodes and/or lesioning techniques cause suffering, and data interpretation is hampered by species differences.

The Trust helped validate **magnetoencephalography (MEG)** in the 1990s, as applied to visual processing and epilepsy in volunteers (7). MEG has very high temporal and spatial resolutions, and can be used multi-modally with fMRI and EEG. MEG studies have generated invaluable data about human brain function (8).

Diffusion tensor imaging (DTI) is a novel advanced technology used to study deep white matter in the brain. The Trust quickly recognised the technique's potential to replace tract-tracing and electrode experiments in animals (9). Our reseach applies DTI quantitatively to analysing human brain networks (10) and their breakdown in illnesses, such as chronic pain disorders.

The Trust also supported research using **transcranial magnetic stimulation (TMS)** to simulate brain damage in volunteers. Reversible 'virtual' lesions are created to study the function of the targeted area and its interactions with other brain regions. Novel information about human brain function in visual, motor and learning tasks has been discovered (11).

7. Fylan F et al (1997). NeuroImage 6:47-57.
8. Hall SD et al (2005). NeuroImage 26:13-17.
9. Langley G (2004). Going with the flow. Dr Hadwen Trust Science Review, p 22.
10. Johansen-Berg H et al (2005). Cereb. Cortex 15:31-39.
11. Rushworth MFS et al (2001). Nature Neurosci. 4:656-661.

The Dr Hadwen Trust has 37 years' experience of supporting high-quality, peer-reviewed and innovative research to replace animals in a wide range of medical fields. The Trust also actively promotes the concept and implementation of replacement techniques.

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