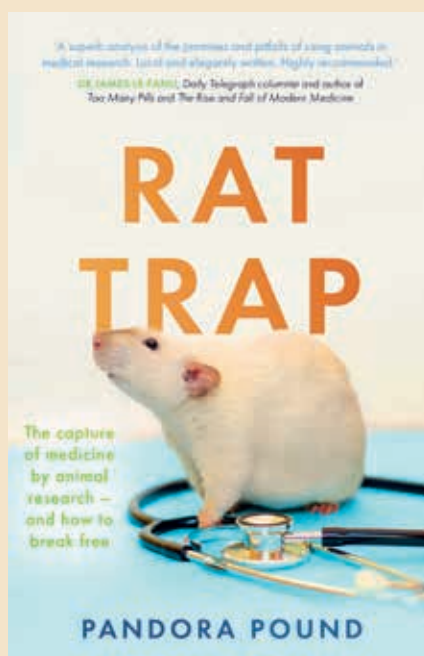


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animals used in research at the medical school. Pound recounts vividly the secrecy that shrouded animal research in the 1990s, the closed doors, covered cages, discouraged conversations. But it was this experience that ultimately led Pound, who has a PhD in the Sociology of Medicine, to question what, if anything, had research on animals contributed to human medicine, and her book is the culmination of her work on it over the past 25 years.

Research on animals remains a controversial subject but, focusing on the science rather than the ethics, Pound provides a riveting, accessible account of how the paradigm became so well established and 'locked in' to pharmaceutical development and academia, before revealing how a lack of evidence to support its effectiveness has resulted in poor translational rates from animal studies to human medicine, ultimately failing us all.

In 2004 Pound, who is now Research Director for the Safer Medicine Trust (safermedicines.org), published, 'Where is the evidence that animal research benefits humans?', a now seminal article in the *British Medical Journal*. This piece of work with epidemiologists, who routinely use systematic reviews to analyse the quality of evidence for healthcare decisions, concluded that much animal research into potential treatments for humans is wasted because it is so poorly conducted. The piece was met with hostility 20 years ago, but ultimately the call for increased, formal evaluation of animal research was welcomed.

However, as more animal studies were scrutinised using systematic reviews, it was evidenced that the majority of pre-clinical animal studies were conducted to a low standard with poor adherence to even basic scientific principles – including a lack of blinding and random allocation, inadequate sample size, poor reporting – and were therefore

unable to generate data that could reliably inform human medicine. Ultimately this has led to an overstatement of the validity of animal research, spurious claims of effectiveness and an 'illusion amongst scientists, funders, politicians and members of the public that animal research works better than it does'. We are thus caught in the Rat Trap.

This is a revelation and, as Pound forensically dismantles the animal research myth, an empirically substantiated work, she concludes: 'Animal research is impeding medical progress and wasting resources, resulting in an enormous unmet need for patients.' Indeed there is. The 'success' rate of new candidate drugs for Alzheimer's is 0.4%, for cancer it is 5.1%, for cardiovascular disease it is 6.6%, for stroke, 0.1%. Other repeated failures of animal models include motor neuron disease, traumatic brain injury, osteoarthritis, Crohn's, asthma, HIV/AIDS, depression, Parkinson's, sepsis and type 1 diabetes.

Additionally, in drug development, prior to human trials, toxicology studies in animals are always used to satisfy regulators and Pound details a 2015 study that compared animal and human toxicology data for over 2,000 drugs. This found that the absence of toxicity in animals was unable to predict an absence of toxicity in humans – if a drug appears safe in animals, it can be toxic to us. Approximately half of drugs removed from the market in Europe and US are withdrawn due to safety issues and a shocking 6.5% of UK hospital admissions are due to drug side effects.

However, whilst animal researchers resist the spectacular failure of animal models to translate, caught in a 'pathological consensus' that it will 'come good' in the end, they try increasingly grotesque ways to 'humanise' animals to model human physiology more closely. Yet, the elephant in the room that is species difference trumps all – differences in gene expression between humans and animals – cannot be overcome.

So why has the animal research paradigm endured despite its proven limitations? Pound details a mixture of vested financial interests (the breeding of animals, cages, restraints and devices for use in labs is big business), grant funder bias toward animal data, as well as scientific conservatism, conformity and inertia. Crucially, regulatory dysfunction is key: 'Insufficient expertise, inadequate scrutiny, scientific self-interest and regulatory capture' are all thwarting the transition to human biology-focused drug development, says Pound. In 2017 not one of the 587 applications to conduct

RAT TRAP

The capture of medicine by animal research and how to break free

by Dr Pandora Pound

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Reviewed by Claire Colley

In this book Dr Pandora Pound recounts her daily walk to her offices in London's St Thomas's Hospital, passing through Block Nine that held the

animal research was rejected by the Home Office, despite legislation requiring adherence to the 3Rs principle, a futile tick-box exercise.

However, as more and more scientists move away from animal models, Pound offers some qualified hope. Developments in human cell and genome biology, 3D cell cultures, organ on a chip, *in silico* modelling and more are truly exciting and, while not yet perfect, many already far outperform animal tests. 'Using animals is now preposterous' says Pound, a conclusion it is difficult to disagree with and, as she notes in her recent article (*BMJ* 2024;386:q1600) 25 years on from her first, hopes are high that the new Labour Government will deliver on its promise to phase out animal testing: 'It's time to pull the plug', says Pound.

An enthralling, must-read book on one of the most urgent topics of our times.

Claire Colley is a London-based journalist. She works in investigations, documentary filmmaking and has written for many major UK publications, including The Guardian and Observer, The Independent and The Times.
