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Oxford Vivisectionists are Swimming Against the Tide

Marius Maxwell

As a neurosurgeon and neuroscientist with two decades of research experience, I feel qualified to contribute to the debate on non-human primate vivisection. The arguments of the Weatherall Committee defy much current scientific evidence, and have served only to confirm my view that the data supporting non-human primate vivisection are profoundly flawed and together with the moral case are indefensible.

I concur with the findings of the crucial Perel study in the December 15th (2006) issue of the British Medical Journal (www.bmj.com), which represents a comprehensive and quantitative statistical meta-analysis to test the usefulness of a broad spectrum of animal based drug testing in predicting human outcomes. This analysis, which undermines the conclusions of the Weatherall Committee, found that only three of the six categories actually succeeded in predicting the results of subsequent human trials and that in all animal experimentation studied "the quality of the experiments was poor." No better than the toss of a coin in other words. The predictive power may actually be even worse, since the study found evidence of broad publication bias in those experiments that did predict human outcome. They concluded that "Discordance between animal and human studies may be due to bias or to the failure of animal models to mimic clinical disease adequately."

It is important to bear in mind that these six areas represent a vast cross section of animal based drug studies including stroke, head injury, systemic haemorrhage, neonatal respiratory distress and osteoporosis. A total of 228 published animal studies were evaluated representing many thousands of animal test subjects including non-human primates. This is only the last in a long series of studies critical of the predictive ability of animal experimentation to human health care with some yielding concordance rates as abysmally low as 5 per cent.

The ultimate effect of such imprecise animal-based research is reflected in tens of thousands of unnecessary human deaths before the responsible drugs are finally withdrawn. Examples include the use of steroids in human head and spinal cord injury; amrinone for heart failure; hormone replacement therapy (which is still in use) and Vioxx - the word's greatest ever drug catastrophe, which killed up to 140,000 people between 2000 and 2004. Other drugs have been abandoned before reaching the market, after harming or failing to help volunteers in human trials. Examples include TGN1412 at Northwick Park hospital; an Alzheimer's vaccine in 2001; and 80 HIV/Aids vaccines which have failed in over 100 clinical trials, despite prior testing in non-human primates on a massive scale. The gratuitous use of non-human primates in much psychological and behavioural laboratory experimentation does, based on my review, infrequently fall short of scandalous. Alternative, state of the art non-animal-based methods of accurately predicting drug safety include microdosing and in vitro assays, human DNA chips, and virtual human organs.

The Weatherall Committee stated that research on animals, including non-human primates, might alleviate "continued suffering to very large numbers of humans..." But it is now clear that the use of animals in drug-screening is actually endangering countless human lives. Extensive, unbiased, and dispassionate meta-analyses of the accuracy and validity of animal research should be the only yardstick employed in this debate.

Doctors, pharmacists, and patients groups in the Netherlands are now demanding government action after a national study has found that drug related problems caused twice as many hospital admissions as motor vehicle accidents (www.bmj.com, 15th December 2006). The December 13th (2006) issue of Nature (www.nature.com) also has a timely but troubling review of animal research and demonstrates that the tide is changing inexorably against animal vivisection. There is discussion of the recent (December 2005) Swiss reform of an animal welfare law to protect the "dignity of creation" of animals. This rightly has had the effect of progressive denial of funding for non-human primate research.

Many are fond of claiming the importance of animal research to early scientific discoveries as if the same historical models bear any relevance at all to contemporary science. Obviously animal research in the past century, in the absence of better alternatives, has benefited mankind as did ancient studies of human anatomy. Michelangelo's anatomical drawings and William Harvey's description of human circulation spring to mind, but who would seriously argue that cadaveric dissection represents cutting-edge science today?

The field of Parkinson's Disease (PD) research was greatly stimulated by the therapeutic attempts of neurosurgeons using dopaminergic brain transplantation in animals and humans which came to the fore

in the 1980's and have since largely receded. There have been too many false positives to record here. Many possible false negatives may also have been ignored as part of widely documented publication bias. The most common non-human primate model of PD results from monkeys being poisoned with the neurotoxin MPTP. It is widely acknowledged that profound disparities (anatomical, physiological, neurochemical, pathological, and temporal) exist between the MPTP non-human primate model and humans with idiopathic PD. Despite these paramount concerns of human reproducibility, hundreds of studies involving thousands of animals have followed with conflicting and non-predictive results. There is no evidence to suggest that their overall predictive concordance to human PD treatment, if subjected to the meticulous quantitative analyses of Perel and co-workers above, would exceed the best case 50:50 coin toss probability established.

Neurosurgeons have employed precise coordinated stereotactic techniques in the treatment of PD, with subtle variations in deep brain nuclear targets, since the 1950s based on human observation. The technique of deep brain stimulation (DBS) was discovered through experimentation in patients with PD (not in animals) in 1987. Though not a cure for PD, it does ameliorate some of the symptoms and is accompanied by a troubling incidence of depression, often suicidal. It is important to understand that ethical clinical research of actual consenting end stage human PD patients themselves has been conducted now for decades. Those are precisely the results that can be accurately translated to other human sufferers. Although researchers have rushed to duplicate and extend these studies in the neurotoxin non-human primate models, I am not persuaded that the nuances in deep brain nuclear therapeutic identification could not have been more accurately identified in the very PD patient cohorts which gave rise to the technique of DBS itself.

As an Oxford graduate I am appalled by the decision of Oxford University to proceed with the construction of the animal research laboratory on South Parks Road. They are swimming against the tide of international medical and ethical opinion. I fear that history will judge their animal rights opponents as less extreme than the very scientists who persist in non-human primate research in the face of an increasing body of consistent and compelling evidence that the resulting data has and will continue to endanger countless human lives.

The spectacle of a minority of Oxford animal researchers tirelessly promoting their claimed achievements before the media has caused me deep unease. They have surprisingly gone on record in backing the use of animals in cosmetic testing and urging the return to the use of great apes in experimentation, activities which have been illegal in the UK for many years. In my experience, the humility and reticence characteristic of truly eminent scientists precludes such behaviour and the protagonists should understand that because of obvious bias they should be the very last people to loudly judge the merits of their own work. The recent BBC2 documentary (Monkeys, Rats and Me, 27th November, 2006) on non-human primate vivisection was wholly emotional and lacking in any truly scientific balance or objectivity. I found the images of severely affected patients being presented to back their doctor's various therapeutic assertions to be regrettable. This is not the way to present a controversial scientific case for critical public evaluation. Many of my Oxford colleagues in world-class scientific laboratories, and in the humanities, are privately aghast at the ability of a small group of media-savvy vivisectionists to hold the debate hostage and thereby besmirch the international reputation of their University. They are unwilling to broadcast their opinions because of the perceived danger of recrimination by the University and funding bodies.

The techniques and language of frontier-breaking molecular genetic technology, for example, are largely unintelligible to those unschooled in their use and therefore pose hurdles to inter-disciplinary scientific understanding. This may be an explanation for why many vivisectionists are not fully aware of all the applicable developments in other facets of enquiry into the same disease and seem overly anxious to declare emphatically and prematurely that no alternatives to non-human primate research can conceivably exist in the foreseeable future. You may add to this the natural human reluctance of animal researchers to turn their back on many years of endeavour and learn anew contemporary scientific protocols.

British neurosurgical colleagues of mine have expressed concerns that the acrimonious debate over non-human primate vivisection and functional neurosurgery (such as DBS) at Oxford has begun to detract from and overshadow many other achievements of their profession. DBS is an important and successful adjunct to the treatment of PD, is derived from experimentation on human subjects, and helps less than 1% of all neurosurgical patients. They are also worried about the wisdom and balance of allocation of precious financial resources within the cash-strapped NHS and medical research sectors.

The 'spin' perpetuated by overly credulous and biased media reporting that opponents of animal experimentation are 'anti-science Luddites' is hollow. How on earth can an animal researcher still claim to be pro-science while wilfully ignoring the vast body of current evidence undermining broad swathes of animal research? It is extraordinary how many media reports of the significance of recent studies casting doubt upon the accuracy and reliability of animal research are casually undermined by the irrelevant assertion that they will only serve as grist to the mill for "animal rights activists." Surely the end-point of the debate should be human safety. Simply stated, the fact of the matter is that animal research in general has now been revealed to be dodgy science which ultimately endangers human lives.

The debate is further muddied by the strident claims of dubious 'citizens' groups. Their sources of funding should be scrutinised before their claims of legitimacy can be believed. This activity is reminiscent of the tactics employed by tobacco companies to cast doubt and aspersions upon the vital causal link established between cigarette smoking and lung cancer by the Oxford epidemiologist Sir Richard Doll in 1950. By deliberately delaying the societal recognition of the dangers of smoking for decades, untold deaths were caused. Parallels with tobacco litigation are being developed by various plaintiffs' lawyers involved in class action suits against drug manufacturers and will demonstrate that the latter have long been aware of the dangerous imprecision of animal drug testing models to human outcomes thereby making them liable for punitive damages.

History has a tendency of repeating itself, I thought, as I recently read the scathing report of the planning inspector who conducted the public enquiry into Cambridge University's controversial primate laboratory in 2002. He concluded that no national need for brain research on primates had been demonstrated. Cambridge University wisely cancelled the project. The economic reasons for non-human primate research, while obvious and most lucrative are shortsighted and damaging, and are no more compelling now than they were in 2002. Research and development of more accurate and more ethical alternatives will easily fill the income shortfall to the University following a much-needed moratorium on non-human primate research.

I would urge that the South Parks Road building be made into a world-class medical imaging and research centre. The explosion of imaging techniques over the past decade (functional MRI being but one) has alone obviated the need for non-human primate vivisection especially in the neurosciences. Humans can and are being studied in ways that would have been unimaginable only ten years ago. The eighteen million pounds for the animal research building could be better spent by Oxford University with a more inspired, rational and forward-looking appreciation of the trajectory of medical research technology.

It is clear to anyone who cares to study the matter closely, honestly and objectively that the scientific justification for non-human primate vivisection is unsound. I cannot accept that its practitioners really believe it to be morally or ethically defensible either. The argument that supports non-human primate experimentation because of close kinship to humans but, blind to their moral worth, denies them ethical rights is sinister and repugnant. The resigned and credulous "Nasty but necessary" defence of non-human primate research coined by a Guardian Leader (13th December, 2006) is simplistic, naive, and selectively ignores the mountain of conflicting scientific data.

Sadly, history reminds us that doctors and scientists have often been blind to the moral dimensions of their work. It is instructive to recall that only little more than sixty years ago, unspeakable and nightmarish forced human vivisection was performed by the notorious Unit 731 of the Japanese Army during development of their wartime chemical and biological weapons programmes (The Guardian, 27th November, 2006).

The general public, a clear majority of whom is opposed to animal research, deserves to be educated about the dangers of and protected from adverse drug reactions stemming from weak and outdated animal research protocols. If scientists as a group fail to serve society by adequately and transparently policing the dangers and inconsistencies of their own research, parliament will have to step in to insist upon a rigorously objective assessment of all aspects of the drug safety testing process.

Indeed, the Toxicology Working Group of the House of Lords Select Committee on Animals in Scientific procedures in 2002 recommended that "the reliability and relevance of all existing animal tests should be reviewed as a matter of urgency."

Following the recent catastrophic Northwick Park clinical study, 250 MPs (a clear majority of those eligible to do so) signed Early Day Motion 92: "That this House, in common with Europeans for Medical Progress, expresses its concerns regarding the safeguarding of public health through data obtained

from laboratory animals, particularly in light of large numbers of serious and fatal adverse drug reactions that were not predicted from animal studies; is concerned that the Government has not commissioned or evaluated any formal research on the efficacy of animal experiments, and has no plans to do so; and, in common with 83 per cent of general practitioners in a recent survey, calls upon the Government to facilitate an independent and transparent scientific evaluation of the use of animals as surrogate humans in drug safety testing and medical research."

This issue fundamentally turns upon absolute scientific objectivity, integrity and morality. The controversy will continue to afflict the University, will not dissipate and cannot be legislated away. Scientific and non-scientific anti-vivisectionists alike have every right to be heard and to occupy the moral high ground of their esteemed Oxford forebears Johnson, Ruskin and Lewis. The end of non-human primate experimentation is nigh and I suspect that its few remaining adherents well know it. The construction of the South Parks Road animal facility will continue to fester like a "carbuncle on the face of an old friend" until the University finally comes to its senses and has it excised.

"I know not by doing any living dissection any discovery [that] has been made by which a single man is more easily cured," wrote Samuel Johnson the eighteenth century Oxford lexicographer who condemned doctors who "extend the art of torture" by performing research on animals. Time has finally proven the good Doctor right.

Marius Maxwell MBBChir, DPhil
mariusmaxwell1@gmail.com