Self experimentation and in vitro research cannot suffice: A plea for refinement

Summary
In their comments on my article published in ALTEX, Lindl et al. as well as Deutsch purport that self experimentation and in vitro investigation are preferable to animal experimentation because important discoveries result from these two approaches. Regrettably, this is not the case. Instead, history proves that many heroic self experiments of the past were highly dangerous and the results obtained were only useful to mankind because either before or afterwards intensive animal experimentation took place. Even important in vitro observations, e.g., the antibacterial effect of Penicillium notatum, require intensive animal experimentation before they can be made useful to mankind. Therefore, in addition to self- and in vitro experimentation, the implementation of more refinement should be achieved by joint efforts of serious scientists and lay people involved in animal protection.

Zusammenfassung: Selbstversuche und in vitro Forschung reichen nicht aus: Ein Plädoyer für mehr „Refinement“

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It is unfortunate that a constructive dialogue between scientists who are open to animal protection and (professional) animal protectors is commonly prevented by intentional misunderstanding. Without a doubt animals would benefit most if both sides strove for consensual improvements. To suggest that the other has dishonourable intentions and to call him/her names such as "wolf in a sheepskin" is to renounce the possibilities of cooperation. Currently, many universities are fighting for chairs for the further development and implementation of the 3R principle. These universities need support. It does not help to claim that all animal experiments are unnecessary, outdated and can be replaced by cell culture methods, computer simulations and self experimentation. It is because I use all three alternatives and have participated in the development of some (e.g. Brune et al., 1981; Hummel et al., 1993; Bang et al., 1995; Tegeder et al., 1999) that I can point out that these methods do not always suffice to protect the consumer and to achieve relevant, useful research results. That is why I would like to answer some of the comments of the authors T. Lindl, M. Schmitt and M. Völkel as well as M. Deutsch on my article in ALTEX 19, 3, 2002:

The authors Lindl et al. say that the most significant Medical Nobel Prizes were awarded for self experimentation. Unfortunately, the opinion of the authors that self experimentation is more important than animal experimentation is not only wrong but dangerous. Of course, committed scientists have often experimented on themselves and have sometimes even made important discoveries. We often test pain killers on ourselves, but only when our ethical board permits this. Self experiments without permission used to be performed more commonly – often with dangerous consequences. It will remain unclear how many scientists died or were left with permanent injuries. Some reports on such experiments, which almost ended in death, are accessible:

The microbiologist von Pettenkofer from Munich wanted to convince the world that Vibrio cholerae, which was discovered by R. Koch, does not cause cholera. He drank a glass full of culture medium with the bacteria and did not (luckily) become sick. Science did not – correctly – follow his evidence. Embarrassed, he stepped back from his professorship and later committed suicide.

The famous gynaecologist Simpson was more successful. After the discovery of ether he went looking for a very fast narcotic for childbirth. He inhaled all kinds of vapours and gases of different chemicals – however only after testing them on rabbits. One compound, ethidiumdibromide, appeared to work very well. The rabbits fell asleep immediately and woke up again soon afterward. On the next day, Simpson wanted to test this compound on himself. A colleague suggested he first have a look at the experimental animals from the day before. They had died during the night. Without the prior animal experiment this self experiment would probably also have ended in death (Youngson, 1979), and thousands of women would not have benefited from pain treatment during birth, as Simpson discovered chloroform soon afterwards – which was used for decades even by queens (à la reine).

The famous scientific partner of my predecessors in Erlangen, Emil Fischer, who was later awarded the Nobel Prize, performed smelling experiments with newly synthesized (reactive) compounds – many of which were substances which can be metabolised to carcinogenic nitrosamines in the body. He developed stomach problems during these experiments, which held on for many years and possibly contributed to the development of his stomach cancer.

W. Forssmann was, as Lindl et al. state, a Nobel Prize winner and a pioneer of heart catheterisation. However, the development of the heart catheter, which is repeatedly mentioned, by Cournand, Forssmann und Richards did not happen without animal experiments. Although Forssmann pushed a bladder catheter from his elbow into his heart in a heroic self experiment after he had practised on corpses (without the agreement of the relatives!), this single success found no recognition as it had violated the ethical principles of clinical medicine: the dangers of the procedure
were known, the bladder catheter was unsuitable and Forssmann had a family, which he would have left behind without provision if he had had less luck. As we know today, he was very lucky to avoid a thrombosis or heart attack. After this intervention his boss, Ferdinand Sauerbruch, called him a “circus artist” and fired him, also citing ethical considerations. At first, Forssmann’s self experiments had no medical consequences. Only when the Frenchman Courand, together with the American Richards, tested the possibilities and limitations of heart catheterisation and standardised the procedure in numerous experiments on dogs, the foundation for medical application was laid. Forssmann was very lucky to receive the Nobel Prize together with Courand and Richards in 1956.

Finally, Lindl et al. discussed the retired French doctor Pierre Bastien, who saved himself from intoxication with amanita using antibiotics and vitamin C. According to Lindl et al. this occurred in 1981. However, the Swiss pharmacologist G. Floersheim described the successful use of antibiotics to treat poisoning with amanita 10 years previously. He found this therapy in animal experiments, which I myself, then in Basel, participated in (Floersheim, 1974).

The award of the Nobel Prize for Medicine in 1949 to the Portuguese neurosurgeon E. A. Moniz shows where testing on humans without the necessary prior animal experiments can lead. He reported that heavily schizophrenic patients could be extensively healed by severing the nervous tissue leading to the frontal lobe of the brain (lobotomy). He operated on two patients without prior animal experiments and claimed great success. This procedure proved to be unsuitable after a short time. Lobotomised patients suffer fewer delusional attacks, but they spend the rest of their lives hardly responsive and without emotion. It is only right that this procedure has not been used for many decades. The damage done to these patients could have been prevented by prior behavioural experiments on animals.

There are many more such examples. Especially in the early times of scientific medical research there were many cases of self experiments which resulted in long term injuries. That is the reason why modern research guidelines prevent the use of new chemicals and new procedures on humans without prior testing in appropriate systems, such as cell cultures, lower organisms and animals, because it is deemed unethical. An acceptable self experiment usually needs the animal experiment as a basis!

Against this setting the statement of Lindl et al., that many wrong and questionable experiments are undertaken in experimental research, appears banal and trivial. No sensible scientist has or would deny this. Scientists are also human and make mistakes.

Research has drawn the consequences a long time ago: self experiments with new methods and untested substances are also prohibited for doctors. Animal experiments must be authorized and new chemicals must be tested thoroughly before they are used on humans – even cosmetics. Not only scientists but fashionable women must be protected (from their vanity).

Furthermore, the authors also list the well-known so-called ‘Lipobay affair’ as an argument against animal experiments – wrongly. The so-called statins – medical substances which decrease the concentration of cholesterol in the blood – are considered the most valuable therapeutic innovation in the last 20 years. These substances protect numerous older people every day from untimely death. Isn’t it naïve as well as polemic to claim that one of these substances (obviously without sufficient experimental and clinical testing by the manufacturer), given at too high a dose induced life-threatening side effects in only a few patients (about 50)?

This is a group of pharmaceuticals which was developed with the help of animal experiments (not only one!) and that is used with clearly quantifiable success by about a third of all older Central Europeans.

A short word to Markus Deutsch: He appears to believe that one could find antibiotics in a Petri dish and use them on humans without any animal experiments. Perhaps he does not know that the first successful antibiotic substance, Prontosil rubrum (synthesized by Domagk), could not have been identified as antibacterial without an animal experiment (Domagk, 1935). Its effective metabolite – the first sulphonamide – is only released in the intact organism, i.e. not in the Petri dish. The discovery of the sulphonamides resulted from animal experiments (Domagk, 1935).

The case is similar regarding penicillin. A. Fleming did observe that a component of the fungus "Penicillium notatum" inhibits the growth of bacteria. But only the isolation, purification and stabilisation in Florey’s group with the help of numerous experiments on mice and dogs (Chain et al., 1940) led to the first application of penicillin in humans – no chemotherapeutics without animal experiments! Or the other way around: in vitro research (also with the help of cell cultures) is useful and helps to reduce animal experiments – however, until now it cannot fully replace animal experiments as a basis for the application of new chemicals (pharmaceuticals)!

These few examples shall suffice. The aim of this text is not to reproach others for their ignorance. Instead we should stop making bold claims which, although convincing at first, comprise little truth. It fills me with worry that research on the 3R principle, which has been furthered by many successful scientists, is not noted by the authors Lindl et al., or is put off as outdated. Worldwide, numerous scientists – not only some of my colleagues and I – have endeavoured successfully to replace animal experiments in research and education by means of cell culture methods (Brune et al., 1981; Bang et al., 1995), self experiments (authorized by the ethical commission (Tegeder et al., 1999)) and computer simulations (Hummel et al., 1993). Apparently, Lindl from the (private) Institute for Applied Cell Culture thinks that innovative, 3R conform research only takes place in his environment – sadly using organs (e.g. Lindl, 1983) and cells (e.g. Lindl and Chapman, 1976) from “consumed” animals – still a step forward, as Lindl himself still conducted “simple” animal experiments in 1975 (Kießling et al., 1975).

Is his letter to the editor only a marketing trick? I hope not. It also does not help that Lindl repeats his reservations about the applicability of animal experiments, published in ALTEX 18, 3, 2001, and informs us all of additional insights from a personal experience. One of these is that, in 1975 (Kiessling et al., 1975), he still conducted “simple” animal experiments in 1975 (Kießling et al., 1975).

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References


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