

A comprehensive, referenced list of the most famous failures of animal models and testing, which have had fatal consequences for human patients.

1. Smoking was thought non-carcinogenic because smoking-related cancer is difficult to reproduce in lab animals. Many continued to smoke and to die from cancer.[2]

2. Benzene was not withdrawn from use as an industrial chemical despite clinical and epidemiological evidence that exposure caused leukemia in humans, because manufacturer-supported tests failed to reproduce leukemia in mice.[1]

3. Animal experiments on rats, hamsters, guinea pigs, mice, monkeys, and baboons revealed no link between glass fibers and cancer. Not until 1991, due to human studies, did OSHA label it carcinogenic.[3][4][5]

4. Though arsenic was a known human carcinogen for decades, scientists still found little evidence in animals to support the conclusion as late as 1977.[6] This was the accepted view until it was produced in lab animals.[7][8][9]

5. Many continued to be exposed to asbestos and die because scientists could not reproduce the cancer in lab animals.

6. Pacemakers and heart valves were delayed in development because of physiological differences between animals they were designed on and humans.

7. Animal models of heart disease failed to show that a high cholesterol/high fat diet increases the risk of coronary artery disease. Instead of changing their eating habits to prevent the disease, people continued their lifestyles with a false sense of security.

8. Patients received medications that were harmful and/or ineffective due to animal models of stroke.

9. Animal studies predicted that beta-blockers would not lower blood pressure. This withheld their development. [10][11][12] Even animal experimenters admitted the failure of animal models of hypertension in this regard, but in the meantime, there were thousands more stroke victims.

10. Surgeons thought they had perfected radial keratotomy, surgery performed to enable better vision without glasses, on rabbits, but the procedure blinded the first human patients. The rabbit cornea is able to regenerate on the underside, whereas the human cornea can only regenerate on the surface. Surgery is now performed only on the surface.

11. Combined heart lung transplants were also "perfected" on animals, but the first 3 patients all died within 23 days.[13] Of 28 patients operated on between 1981 and 1985, 8 died peri-operatively, and 10 developed obliterative bronchiolitis, a lung complication that the experimental dogs did not get. Of those 10, 4 died and 3 never breathed again without the aid of a respirator. Obliterative bronchiolitis turned out to be the most important risk of the operation.[14]

12. Cyclosporin A inhibits organ rejection, and its development was watershed in the success of transplant operations. Had human evidence not overwhelmed unpromising evidence from animals, it would never have been released.[15]

13. Animal experiments failed to predict the kidney toxicity of the general anesthetic methoxyflurane. Many people lost all kidney function.

14. Animal experiments delayed the use of muscle relaxants during general anesthesia.

15. Research on animals failed to reveal bacteria as a cause of ulcers and delayed treating ulcers with antibiotics.

16. More than half of the 198 new medications released between 1976 and 1985 were either withdrawn or relabeled secondary to severe unpredicted side effects.[16] These side effects included complications like lethal dysrhythmias, heart attacks, kidney failure, seizures, respiratory arrest, liver failure, and stroke, among others.

17. Flosint, an arthritis medication, was tested on rats, monkeys and dogs; all tolerated the medication well. In humans, however it caused deaths.

18. Zelmid, an antidepressant, was tested on rats and dogs without incident. It caused severe neurological problems in humans.

19. Nomifensine, another antidepressant, was linked to kidney and liver failure, anemia, and death in humans. Animal testing had given it a clean, side effect-free bill of health.

20. Amrinone, a medication used for heart failure, was tested on numerous animals and was released without trepidation. Humans developed thrombocytopenia, a lack of the type of blood cells that are needed for clotting.

21. Fialuridine, an antiviral medication, caused liver damage in 7 out of 15 people. 5 eventually died and 2 more needed liver transplants.[17] It worked well in woodchucks.[18][19]

22. Clioquinol, an antidiarrheal, passed tests in rats, cats, dogs and rabbits. It was pulled off the shelves all over the world in 1982 after it was found to cause blindness and paralysis in humans.

23. Eraldin, a medication for heart disease, caused 23 deaths despite the fact that no untoward effects could be shown in animals. When introduced, scientists said it noted for the thoroughness of the toxicity studies on animals. It caused blindness and deaths in humans. Afterwards, scientists were unable to reproduce these results in animals.[20]

24. Opren, an arthritis medication, killed 61 people. Over 3500 cases of severe reactions have been documented. Opren had been tested on monkeys and other animals without problems.

25. Zomax, another arthritis drug, killed 14 people and caused many more to suffer.

26. The dose of isoproterenol, a medication used to treat asthma, was worked out in animals. Unfortunately, it was much too toxic for humans. 3500 asthmatics died in Great Britain alone due to overdose. It is still difficult to reproduce these results in animals.[21][22]
[23][24][25][26]

27. Methysergide, a medication used to treat headaches, led to retroperitoneal fibrosis, or severe scarring of the heart, kidneys, and blood vessels in the abdomen.[27] Scientists have been unable to reproduce this in animals.[28]

28. Suprofen, an arthritis drug, was withdrawn from the market when patients suffered kidney toxicity. Prior to its release researchers had this to say about the animal tests:[29][30] "...excellent safety profile. No ...cardiac, renal, or CNS [central nervous system] effects in any species."

29. Surgam, another arthritis drug, was designed to have a stomach protection factor that would prevent stomach ulcers, a common side effect of many arthritis drugs. Although promising in lab animal tests, ulcers occurred in human trials.[31][32]

30. Selacryn, a diuretic, was thoroughly tested on animals. It was withdrawn in 1979 after 24 people died from drug induced liver failure.[33][34]

31. Perhexiline, a heart medication, was withdrawn when it produced liver failure that had not been predicted by animal studies. Even when they knew they were looking for a particular type of liver failure, they could not induce it in animals.[35]

32. Domperidone, designed as a treatment for nausea and vomiting, made human hearts beat irregularly and had to be withdrawn. Scientists were unable to reproduce this in dogs even with 70 times the normal dose.[36][37]

33. Mitoxantrone, a treatment for cancer produced heart failure in humans. It was extensively tested on dogs, which did not manifest this effect.[38][39]

34. Carbenoxalone was supposed to prevent formation of gastric ulcers but caused people to retain water to the point of heart failure. After scientists knew what it did to humans they tested it on rats, mice, monkeys, rabbits, without reproducing this effect. [40][41]

35. Clindamycin, an antibiotic, causes a bowel condition called pseudomembranous colitis. It was tested in rats and dogs every day for one year. They tolerate doses 10 times greater than humans.[42][43][44]

36. Animal experiments did not support the efficacy of valium-type drugs during development or after.[45][46]

37. Pharmacia & Upjohn discontinued clinical tests of its Linomide (roquinimex) tablets for the treatment of multiple sclerosis after several patients suffered heart attacks. Of 1,200 patients, 8 suffered heart attacks as a result of taking the medication. Animal experiments had not predicted this.

38. Cylert (pemoline), a medication used to treat Attention Deficit Hyperactive Disorder, caused liver failure in 13 children. Eleven either died or needed a liver transplant.

39. Eldepryl (selegiline), a medication used to treat Parkinson's disease, was found to induce very high blood pressure. This side effect has not been seen in animals, where it is used to treat senile dementia and endocrine disorders.

40. The diet drug combination of fenfluramine and dexfenfluramine was linked to heart valve abnormalities and taken off the market although animal studies had never revealed heart abnormalities."^[47]

41. The diabetes medication troglitazone, better known as Rezulin, was tested on animals without significant problems, but caused liver damage in humans. The company admitted that at least one patient had died and another had to undergo a liver transplant as a result.^[48]

42. The plant digitalis has been used for centuries to treat heart disorders. However, clinical trials of the digitalis-derived drug were delayed because it caused high blood pressure in animals. Human evidence overrode. As a result, digoxin, an analogue of digitalis, has saved countless lives. Many more could it have survived had digitalis been released sooner.^{[49][50][51][52]}

43. FK 506, now called Tacrolimus, is an anti-rejection agent that was almost shelved before proceeding to clinical trials due to severe toxicity in animals. ^{[53][54]} Animal studies suggested that the combination of FK 506 with cyclosporin might prove more useful.^[55] In fact, just the opposite proved true in humans.^[56]

44. Animal experiments suggested that corticosteroids would help septic shock, a severe bacterial infection of the blood.^{[57][58]} Unfortunately, humans reacted differently. This treatment increased the death rate in cases of septic shock.^[59]

45. Despite the ineffectiveness of penicillin in his rabbits, Alexander Fleming used the antibiotic on a very sick patient since he had nothing else to try. Luckily, Fleming's initial tests were not on guinea pigs or hamsters, it kills them. Howard Florey, the Nobel Prize winner credited with co-discovering and manufacturing penicillin, stated: "How fortunate we didn't have these animal tests in the 1940s, for penicillin would probably never been granted a license, and possibly the whole field of antibiotics might never have been realized."

46. Fluoride was withheld as a cavity preventative initially because it caused cancer in rats.[60][61][62]

47. The notoriously dangerous drugs thalidomide and DES were tested in animals and released. Tens of thousands suffered and died as a result.

48. Animal experiments misinformed researchers about how rapidly HIV replicates. Based on this false information, patients did not receive prompt therapies and their lives were shortened.

49. Animal-based research delayed the development of the polio vaccine, according to Dr. Albert Sabin, its inventor. The first rabies and polio vaccines worked well on animals but crippled or killed the people who tried them.

50. Researchers who work with animals have succumbed to illness and death due to exposure to diseases that though harmless to the animal host (such as Hepatitis B) but kill humans.

Time, money, and resources devoted to these experiments could have gone to human-based research. Clinical studies, in vitro research, autopsies, post-marketing drug surveillance, computer modeling, epidemiology, and genetic research pose no hazard to humans and provide accurate results. Importantly, animal experiments have exhausted resources that could have been dedicated to educating the public about health hazards and health maintenance, therein diminishing the incidence of disease that require treatment.

REFERENCES:

[1]Sax, N. Cancer-causing Chemicals Van Nostrand 1981

[2]Lancet, June 25, 1977 p1348-9

[3]The Guardian, July 20, 1991

[4]Occupational Lung Disorders, Butterworth 1982

[5]Toxicology & Industrial Health, 1990, vol.6, p293-307

[6] J Nat Cancer Inst 1969, vol.42, 1045-52

[7] Br J Cancer, 1947, vol.1, p 192-251

[8]Advances in Modern Toxicology, vol.2, Wiley, 1977

[9]H Nat Cancer Inst, 1962, vol.5, p 459

[10]Fitzgerald, D. The development of new cardiovascular drugs in Recent Developments in Cardiovascular Drugs eds. Coltart and Jewitt, Churchill Livingstone 1981

- [11] Perspectives in Biology & Medicine, 1980 Part 2, S9-S24
- [12] Pharmacy International Feb. 1986; p33-37
- [13] Lancet, i, p 130-2, 1983
- [14] Lancet, 1, no. 8480 p 517-9, March 8, 1996
- [15] Annals of Internal Medicine 1984, vol.101, 667-682
- [16] GAO/PEMD-90-15 FDA Drug Review: Postapproval Risks 1976-1985
- [17] NEJM 333;1099-1105, 1995
- [18] J NIH Res, 1993, 5, 33-35
- [19] Nature, 1993, July 22, p 275
- [20] Nature, 1982, April 1, p 387-90 and Br Med J, 1983, Jan 15, p 199-202 and Drug Monitoring, 1977 and Pharmacologist, 1964, vol. 6, p 12-26 and Pharmacology: Drug Actions and Reac and Advances in Pharm, 1963, vol. 2, 1-112 and Nature, 1982, April 1, p 387-390
- [21] Pharmacologist, 1971, vol.18, p 272
- [22] Br J of Pharm 1969 Vol. 36; p35-45
- [23] Inman, W. H. Monitoring for Drug Safety, MTP Press, 1980
- [24] Am Rev Resp Diseases, 1972, vol.105, p883-890
- [25] Lancet, 1979, Oct.27, p 896
- [26] Toxicology and Applied Pharmacology 1965, vol. 7; p1-8
- [27] Animal Toxicity Studies: Their Relevance for Man, Quay Pub. 1990
- [28] Br Med J, 1974, May 18, p 365-366
- [29] Drug Withdrawl from Sale PJB Publications, 1988
- [30] Pharmacology, 1983, vol.27 (suppl 1), 87-94 and FDA Drug Review:
- [31] Postapproval Risks 1976-1985 (US GAO April 1990
- [32] Gut, 1987, vol.28, 515-518
- [33] Lancet, Jan 10, 1987, 113-114
- [34] Toxicolo Letters, 1991, vol.55, p 287-93
- [35] Drug Withdrawl from Sale, PJB1988
- [36] Reg Tox & Pharm, 1990, vol.11, 288-307 and Postgraduate Med J, 1973, vol.49, April Suppl., 125-129 and 130
- [37] Drugs, 1982, vol.24, p 360-400
- [38] Animal Toxicity Studies Quay, 1990
- [39] Lancet, 1984, July 28, p 219-220
- [40] Matindale: The Extra Pharmacopoeia, 29th edition, Pharmaceutical Press, 1989)
- [41] Br Nat Form, no.26, 1993
- [42] Reg Tox & Pharm, 1990, vol.11, p 288-307
- [43] Br Med J, 1983, Jan 15, p 199-202
- [44] Br Nat Form, no.26, 1993
- [45] Tox & Appl Pharm, 1972, vol. 21, p 516-531
- [46] The Benzodiazepines MTP Press 1978

- [47]Drugs and Therapeutics Bulletin,1989, vol.27, p 28 as quoted in Activate For Animals Oct. 1997 The American Antivivisection Society
- [48]Parke-Davis letter dated Oct. 31, 1996
- [49]Sneider, W. Drug Discovery: The Evolution of Modern Medicine Wiley, 1985
- [50]Lewis, T. Clinical Science Shaw & Sons Ltd. 1934
- [51]Federation Proceedings 1967, vol.26, 1125-30
- [52]Toxicology In Vitro 1992, vol.6, 47-52
- [53]JAMA, 1990, April 4, p1766
- [54]Lancet,1989, July 22, p 227
- [55]Lancet, 1989, Oct 28, p1000-1004 [56] Hepatology,1991, vol.13, 1259-1260
- [57]Drugs and Therapeutics Bulletin, 1990, vol.28, p 74-75
- [58]Anesthesiology: Proceedings of the VI World Congress of
- [59]Anesthesiology, Mexico City 1977
- [60]NEJM, 1987, Sep. 10, p 653-658
- [61]The Causes of Cancer, 1981, Oxford Press
- [62]J NIH Res, 1991, vol.3, p46
- [63]Nature, 1991, Feb 28, p732