HOW MIRACLE DRUGS ARE BORN

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At one time new drugs were found by accidental discoveries of their peculiar effects in man. Thus:

"Quinine" was discovered because a cinchona tree fell into a pond near an Indian village and a brave too sick to travel farther for better water drank the bitter water and got well.

"Ergot" was discovered because tainted rye produced abortion in the poorer classes that could not afford better flour for their bread.

"Digitalis" was discovered because an early physician listened to an old woman's tale of a treatment for dropsy.

"Atropine" was discovered by a pharmacist's apprentice named Daries who rubbed his eye while filling a prescription.

"Strophanthus" was discovered because the botanist on Livingston's expedition to Africa kept his toothbrush in the same pocket with some poisoned arrows.

"Epsom salt" was discovered by a farmer who had a spring on his property from which his cattle refused to drink. He drank and the pharmacological effects were promptly called to his attention.

"Veratrum," which has a strong parasympathetic stimulant effect, was discovered by the shepherd boy Melampe who noted that his sheep developed violent diarrhea after eating the plant called hellebore.

"Acetanilid" was discovered accidentally by one of Professor Kussmanka's assistants who took the compound and noted a drop in his body temperature—undoubtedly with some degree of cyanosis.

"Epinephrine" was discovered because Oliver made extracts of various tissues
of the human body and injected them subcutaneously into his own son. He dis-
covered than an extract of the adrenal gland was the only tissue extract which
accelerated and hardened his son's pulse.

Such rash human experimentation is at best futile and at worst fatal. The
Nazi physicians under Hitler's orders tried many human experiments. The
mortality was high and the scientific knowledge almost nil.

Fortunately, since the turn of the century, most new drugs have been newly-
made chemically and carefully tested in experimental animals. When the chemist
succeeds in making a new chemical, that is exactly what he has, "only a new
chemical." Then this chemical is turned over to the pharmacologist and its
effect is determined in animals. If the drug action is of interest, then various
species of animals are used to determine if all animals are affected in the
same way. The mouse, rat, guinea pig, cat, dog, and monkey may be used to prove
that the drug has predominantly the same effect in all of these species and
hence may have that effect and "no other toxic action in man."

A chemical thus becomes a drug only when and if someone discovers that it
has an action which will help or cure disease. In other words, the drug must
be tested in living animals.

**The Early and Only Vivisectors**

If we go back to the Nineteenth Century, we find that much of our early
physiological and pharmacological knowledge was gained by operations on living,
unanesthetized animals. Claude Bernard (1813-78) and his predecessor Francois
Magendie (1783-1855) made numerous studies on unanesthetized animals, but then
one must remember that anesthesia was not discovered until 1846 and that prior
to this discovery all surgical operations in man were done with the aid of
strong assistants to hold the pain-racked patients on the operating table. One
must also recall that anesthetic drugs were discovered in man and hence the
study of these agents in animals took many years before the experimenter
could be certain that these pain-killing drugs would not invalidate the
experiments. Such data were accumulated by 1900 so that in the Twentieth Century all experiments in animals can now be conducted without pain to the experimental animal.

Birth of the Antivivisectionists

In the Nineteenth Century, French veterinarians reacted to these painful experiments in animals and were instrumental in organizing the antivivisectionists in Europe. This occurred almost at the same time that medical scientists were learning enough about anesthetics to use anesthesia in all experiments. However, in spite of improvement in animal care and experimentation the antivivisectionists are still with us and represent a vociferous and well organized 3 per cent of the voting population. In contrast to this small minority group, a recent opinion survey showed that 85 per cent of the voters are in favor of turning over to medical, veterinary and dental research and teaching all unwanted, unclaimed stray dogs and cats.

What Perpetuates the Antivivisectionists?

Vivisection is gone, but a few antivivisectionists are still with us! Undoubtedly three factors are involved in the self-perpetuation of the antivivisectionist. The first and most important is "ignorance." Ignorance of biological science is common in this sect of crackpots. Some do not believe in vaccination, the use of insulin or eating meat, but they do wear furs, feathers in their hats, and leather shoes. One stated that rabies in dogs is not a disease but is merely a series of symptoms which result from repeated mistreatment of the dog. One stated that the Nazis, without animal experimentation, were able to make human blood out of stone. Yet another recently stated in Baltimore that the use of penicillin was the greatest cause of postoperative mortality in any operation. Yet another stated that medical scientists should learn as do the "astrologists" by observation instead of experimentation! And the final insult to our intelligence came from an editor who said we should make a mechanical man and test our drugs on him! This to scientists who have not been able to
make even a one-celled form of life. The machines of I.B.M., G.E., or M.I.T. do not compare with the lowest form of life made by God!

Avarice the Second Factor

Business enterprise such as motivates the confidence man may also motivate the antivivisectionist. Public relations experts have been known to discover that a neater and quicker buck can be made by playing upon the heart strings of a gullible public. Thus, a new antivivisection society can be formed in any state or municipality, donations can be solicited and contributions will roll in "to help prevent pet torture." The public loses because medical progress is hindered and the only winner is the secretary or managing director who, with little effort, draws his pay for his organizational and soliciting efforts. Avarice may also be a major factor in the numerous theatrical characters who see and use the antivivisectionists movement as a means of continued publicity when their theatrical careers are over. A few newspapers will allot extensive space to these publicity seekers.

Misplaced Sympathy is the Third Factor

Medical scientists are not sadists or torturers. They are more interested in truly humane movements and the prevention of cruelty to animals than any other group. They are the discoverers of various anesthetics which are routinely used by veterinarians to ease pain in animals and occasionally to provide a painless death for over-age or injured pets. They, however, consider human life and well-being above that of animals, while many antivivisectionists consider the dog or the cat to be more important than children and human life. One antivivisectionist points out that dog spelled backwards reads God and infers that the canine race is thus superior to man, woman and child, which are meaningless when spelled backwards. The scientific discoveries of medical scientists have increased man's expected life span from 47 to 67 years since 1900 and, while the statistics are not available, the scientists' efforts have undoubtedly increased the useful life span of our pets and domestic animals,
also. And yet, the Pitman-Moore Company in Indianapolis has difficulty in obtaining enough unwanted, unclaimed, stray mongrel dogs to make rabies and distemper vaccines and serums to protect and save the lives of our pedigreed pets!

Laws Require Experimentation

The United States Pharmacopoeia requires that 52 drugs be assayed in animals before they are sold for use in man. The Food and Drug Administration acting under authority of the 1938 Food, Drug, and Cosmetic Act requires elaborate animal testing before any new drug can be marketed. Thus, a chemical may be studied from one to five or more years in animals before the conditions for use in man are determined. But even this warranted delay does not compare with the many years that may elapse before a new chemical is tested in living animals and its drug effect discovered.

Thus, Gellmo in 1908 made the first sulfa drug, but it was merely a chemical. The world unwittingly awaited the animal experiments of Domagk when in 1932 he used a sulfa drug to treat mice made sick with virulent germs. The mice did not die and by 1937 the drug sulfanilamide had passed all animal tests and could be cautiously tried in human bacterial infections. The results were nothing less than miraculous. The hemolytic streptococcus is one of the most dangerous of germs. When it caused blood poisoning, previously about three out of four of its victims died. In childbed fever, the toll was approximately one in four, while streptococcal (spinal) meningitis was invariable fatal. All this was now changed. Consider, in retrospect, how many thousands of lives would have been saved if Gellmo, in 1908, had only tried (or had Ehrlich try) his chemical on a few sick mice!

Antihistamines

As a further example of how important drugs are discovered we can cite the example of drugs which counteract histamine. Histamine is ordinarily combined in a harmless inactive form in the body, but when animals or men
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become sensitized to pollen or dusts, this allergy or sensitization results in potent form so that the human being or animal is then subject to all of the actions of histamine which may cause asthma, hives, swelling of the tissues, sour stomach, cramps, headache, fainting, or a persistent and troublesome skin rash.

The scientist has shown by the following tests that this new chemical will counteract histamine. (1) He used the isolated bowel of the guinea pig in a constant temperature bath to show that spasm or cramming induced by histamine could be prevented. (2) He placed groups of treated and untreated guinea pigs in a glass enclosed chamber and allowed a measured amount of histamine mist to be forced into this chamber. The untreated pigs died of asthmatic constriction of their bronchial tubes while the pigs injected with the new chemical remained miraculously unaffected. (3) Knowing that histamine will produce fainting owing to a sudden drop in blood pressure, he further used several anesthetized dogs or cats to see first of all how much drop in blood pressure a standard dose of histamine would produce and second if this reduction could be prevented by the new chemical. In addition, the scientist used all of the known antidotes to histamine, such as adrenalin, ephedrine and aminophyllin, to see if this new chemical was as good as, or better than, the marketed drugs.

Yes, this new chemical was better than these other drugs. Well you say, "Let's try it in patients." No, my friends, not so fast! In spite of all this work, we still have merely a chemical—a promising chemical, I grant you—but not a drug which is ready to use in man. The 1938 Food and Drug Laws were designed to protect mankind against promising brain-children of this type. Well, you say, "What's the delay?" We have 10 per cent of the population with allergic conditions, some of whom may not respond well to ephedrine, and this new chemical is effective orally so that they won't have to be injected with adrenalin. This
new chemical antidotes histamine and has no serious side effects in your animals. The delay, my friends, may amount to one or two years while we feed this chemical to the dog, inject it into the growing rat and mouse, and perhaps even invest $350 to purchase 10 monkeys to see if they lose weight, become anemic, have a serious drop in their white blood cell count, or have any serious damage to the liver or kidneys when injected or fed the chemical for a period of many months.

At least, you say, we can save money by using these monkeys and dogs over again for another drug if they have no alarming symptoms. I see you have naively forgotten the tissue studies. Microscopic examination of all tissues is essential, which means that the animals are painlessly sacrificed and studied microscopically. In addition, the drug application must include 400 clinical cases which show the effect of this new chemical in man. Only then can we start selling the drug for use by the physician and he must be trained carefully in how to use it. In summary you should realize that:

1. The Anticruelty Society of Chicago collects 23,900 dogs and 19,100 cats per year (10 year average) but finds homes for only 3.6 per cent of the dogs and 0.6 per cent of the cats. The rest die in a "euthanasia chamber."

2. If medical schools attempted to raise their own dogs these would cost more than $75 each.

3. By killing 50,000 dogs per year the misguided "humane" organizations in the Chicago area destroyed a potential $3,750,000 citizens' contribution to the heart, cancer and infantile paralysis drives.

4. For many experiments omnivorous dogs are better for medical research than are herbivorous monkeys.

5. The intestinal flora of the dog's intestines are more closely allied to man than are those of any other experimental animal. Thus sulfa drugs and antibiotics must be tested in the dog to determine their sterilizing
6. Pregnant dogs were used to show that the anticoagulant "dicoumarol" may produce fatal fetal hemorrhage if used late in human pregnancy to control abnormal blood clots.

7. Pregnant dogs might show the cause of dietary blindness of premature infants. Which would you prefer? A few blind puppies or more blind babies?

8. In modern times all new anesthetic drugs are first tested in laboratory dogs, and the laboratory dog whether used in teaching or research is anesthetized before surgery and is not "cut up alive."

9. In England, laboratories are licensed to use cats and dogs in medical research. Germany, under Hitler, outlawed the use of the cat and dog and used minority groups of human beings instead. The Nazi results were at best "futile" and at worst "fatal!"

10. The blue baby operation and all cardiovascular surgery has been perfected in the dog. Surgery residents learn these operations by practice on the citizens' unwanted stray dogs.

11. Most of our knowledge of the functions of the brain has been accumulated by research on cats.

12. Our pedigreed dogs, mink and all of our domestic animals have their nutritional and infectious diseases cured by knowledge gained in experimental studies on mongrel dogs.

13. The only animal counterpart of "pellagra" in man is "black tongue" of dogs, which resulted in the discovery of a cure of both these diseases, namely, nicotinic acid (niacin).

14. The K-9 Corps during the war consisted of pedigreed dogs performing tasks too dangerous for man, which tasks are now done valiantly and painlessly by mongrel dogs in the medical laboratory.
15. Federal law rightfully requires that scientists assay both parathyroid hormone and adrenalin in the anesthetized dog before their use in man.

16. Only a vociferous 3 per cent of the population is against animal experimentation, while 85 per cent is in favor of turning unclaimed pound dogs over to the medical schools and research laboratories.

17. The cause of diabetes and its treatment was first discovered in the dog.

18. Bleached white flour was proved by medical scientists to be poisonous for the dog, and the milling industry has voluntarily substituted a nontoxic agent.

19. The anesthetized dog is used to train physicians in the use of the instruments to remove trinkets from children's windpipes.

20. Digitalis and other potent heart drugs are assayed in the cat.

21. The unwanted cat has supplied us with our modern anti-epilepsy drugs and our knowledge of the electrical activity of the brain.

22. Many unwanted dogs are used to make distemper vaccine and serum to prevent and treat distemper in pedigreed dogs.

23. Hookworm infests both man and dog so that new remedies for this infestation are first tested in the dog.

24. Almost all that is known about the stomach, intestine, liver and adrenal gland was learned by use of the dog.

---C. C. Pfeiffer, Ph.D., M.D.---