Drugs and Animal Experimentation

Medicine

Prepared for publication in *Medical Progress*, a journal for laymen, which is now consolidated with the SCIENCE NEWS-LETTER. Other articles edited by the American Association for Medical Progress will appear in these pages from time to time.

By ARTHUR H. HIRSCHFELDER, M. D.

The oldest drugs in use have come down from prehistoric times, their usefulness having been established through experience. The ancients knew the purgative value of the waters from mineral springs; the shrines of Hippocrates (460-370 BC) and other great Greek physicians, who mixed religion with their medicine, were located near mineral springs. The ancient inhabitants of India found out that the seeds of their opium poppy would produce sleep and soothe pain; and so opium was carried to Egypt, Greece and China along all the routes of Old World commerce. The Arabians knew that certain balsams and aromatic herbs contained something that helped the healing of wounds, and they brought these primitive antiseptics to Western Europe; though only in the fiction of Walter Scott were they potent enough to heal infected wounds, as Rebecca cured the wounds of Ivanhoe.

The alchemists experimented with mercury in the hope of turning it into gold. By a fortunate chance they used it successfully in a salve to cure the lice and itch which infested the knights of the Middle Ages. By a still more fortunate accident, this same mercury salve was found to cure the venereal plague fo syphilis, which, whether or not it was introduced into Europe by the sailors of Columbus, was first found to overrun Europe just after the discovery of America.

A drug is a substance which, administered to a patient, will tend to cure disease, allay pain or relieve other symptoms. Each drug therefore must have the properties that can produce definite changes in the workings of the body. The great German pharmacologist Paul Ehrlich, laid down the rule that to be safe for treating human beings, a drug must produce the effect desired with less than one-tenth of the amount that might be dangerous. This rule, ever since the discoveries of Ehrlich, has guided pharmacologists in making drugs better and safer.

In order then to be able to use a drug, we must first find out which of all the substances that compose it are the active ones. This is done by chemical separation or analysis. Then each ingredient must be tested. We must learn just how it acts on each organ of the body, that we may know under what conditions it can be helpful or might be dangerous. We must ascertain how much of it will poison or kill an animal, to avoid administering such a dose to human patients. We must learn whether the dose that will produce the desired effect is too near the dose that would injure or kill the patient; very many substances whose effects indicate that they might be useful, exert those effects only when given in amounts too close to the danger line.

It is clear then that, first of all, we must understand the exact workings of the living body, just as the garage worker understands his automobile and recognizes the meaning of the various knocks and noises of its operation. A man who knew merely what the machinery of an automobile looked like (knew the anatomy) would not be useful unless he knew what it was like when the engine was running (understood its physiology), or in case of trouble, could diagnose what was wrong with it from its symptoms, and from them tell how each part was injured (knew the pathology).

The Basis of Pharmacology

But in addition to being a machine, the human body can repair its tissues and organs by healing, by growing parts anew, or by sealing wounds with scar tissue; and the organs of the human body are often capable of enlarging so as to do the increased work that a chronic disease may require. Hence no physician can learn about the living, running human machine from a dead body. He can learn about the living heart, muscle, nerves, digestive organs, and so on, only by studying them in living human beings or by watching their simplest reactions in living animals. The organs of a human being operate in ways very like the organs of animals; the organs of a diseased patient act much as do those of animals in which similar conditions are experimentally produced. To make the organs of a diseased human being operate more normally, the physician uses drugs which can modify the actions of these diseased organs favorably. It is upon the science of experimental pharmacology that modern treatment rests.

A great heart stimulant, digitalis, the active substance in the common foxglove, was discovered accidentally by an English doctor, William Withering, (1741-1799) about the time of the American Revolution. He found that an old woman in the country made a tea out of a mixture of several herbs, one of which was the foxglove, and that with this decoction she had cured several people who had dropsy and whom he had failed to cure. But Withering thought that his digitalis cured his patients of their dropsy by stimulating the kidneys; this we have since found to be incorrect. Almost a hundred years later, the action of this drug on animals was studied by the English physician, Sir Lauder Brunton, (1844-1916). He found that instead of stimulating the kidneys, it made the hearts of frogs and of dogs beat slower and stronger, and so in modern times it has been used as a heart stimulant. Thousands of men and women live useful lives for ten and twenty years after they would have sunk into their graves but for Lauder Brunton's accurate experiments on dogs, with the drug which Withering had given to the world without knowing just how it acted.

Within the last twenty years this drug has been studied again from a different angle, and still greater benefits to humanity have resulted. A German physiologist, Theodor Wilhelm Engelmann, (1843-1906) had found that by touching the heart of a frog it beat again at once, interrupting the regular rate of its contraction. He touched different parts of these frogs' hearts and made them contract irregularly in many different ways, and then showed that dogs' hearts responded in the same way. Ten years passed, and an English country doctor, James MacKenzie, (1853-) puzzled by the irregular beats of his patients' hearts, began to study their (*Turn to next page*)

Animal Experimentation— *Continued*

pulses. He found that some pulses beat in two-step, some foxtrotted in four-step, some beat at a slow march of half-time, and some were out of step with every step and rhythm. He looked up Engelmann's studies on the frogs' hearts and dogs' hearts and found that the hearts of his patients had acted just as those of Engelmann's animals had done; so he reasoned that the disturbances in his patients' hearts must be quite like those that Engelmann had produced. This gave to physicians an entirely new understanding of hearts that beat irregularly. It was found that some which had been thought serious, were really normal, or represented insignificant disturbances which needed no treatment. This was especially true in many children, whose hearts were a little irregular but who were otherwise perfectly normal.

Relief From Dropsy

Later others studied the exposed hearts of dogs and learned what was wrong when the heart beat entirely out of step with any tune or rhythm. This is the commonest and most dangerous ailment of all (auricular fibrillation). MacKenzie then showed how with digitalis the heart could be made to beat slowly and strongly even though out of step. Next Prof. Cary Eggleston of New York (1884-) together with Prof. Robert Anthony Hatcher (1893-) showed how doses of digitalis large enough to make a doctor of the old days tremble with terror, were quite safe for animals and human beings. With these larger doses, patients panting for breath and swollen with dropsy on one day, were breathing quietly and were free from dropsy on the next, with pulses large, strong and quiet, though still irregular.

In the last few years, Wenckebach, a Dutch professor at Groningen, and Max von Frey in Germany, have shown that such irregular hearts, beating out of step with every rhythm, can be made to snap back and so restore health and comfort, without danger to the mind or body of the patient.

The Adrenal

Almost a hundred years ago an English physician, Thomas Addison (1793-1860), found that a certain disease, in which the patient grows weak and pale and slowly dies, is due to a disturbance or deficiency in the two little pads of yellow tissue which rest above the kidneys and are called the suprarenal or adrenal glands. Little else was known on the subject until in 1895 the English physiologists, Sir Edward Albert S. Schaefer (1853-) and Sir Thomas Oliver, showed that an extract of these glands injected into dogs would stimulate the heart and blood vessels. It remained for an American pharmacologist, Professor John J. Abel 1857-) of John Hopkins, in 1898, to produce the active principles of this gland in pure powdered form, which he called epinephrine. It acted on the heart and blood vessels of dogs in the same way as did the extract of the gland. A little later, the Japanese chemist, Jokichi Takamine, working in America, produced it in a little purer crystalline form, which he called adrenalin, and the Viennese chemist, Pauli, found out just how it can be made in the laboratory.

Epinephrine or adrenalin is the strongest known stimulant for the heart. Injected directly, it sometimes can even revive a heart that has stopped beating. Painted on a bleeding surface, it makes the blood vessels shrink and stop bleeding. A drop put into the nose can shrink up the mucous membrance and relieve a cold or sinus trouble. Injected under the skin, it widens out the bronchi and gives relief for asthma and hay fever. But none of these uses were discovered by trial on human beings alone. It was only after the exact effects had been determined and safe doses had been worked out on living animals that the real uses of adrenalin in medicine could have been found.

Insulin

The sweetbreads of the calf are a delicacy long enjoyed by epicures; but no one suspected that they had any connection with diabetes, the disease in which there is too much sugar in the blood, until in 1889, Oscar Minkowski (1858-) and Joseph von Mering cut the sweetbreads (pancreas) from a dog, and found that the dog acquired diabetes like that in human beings. So they tried to treat diabetes with powdered pancreas just as Schiff had done with the thyroid, but when fed by mouth it was useless, and injected under the skin it was dangerous.

Twenty-five years with thousands of experiments went by, and then a young pathologist, Admont Clark at Johns Hopkins, showed that if salt solution were passed through the blood vessels of a dog's pancreas, this blood would help the heart of a diabetic dog to burn up more sugar. John R. Murlin (1874-) in Rochester, New York, carried these experiments further and found that fluid passed through the blood vessels of a dog's pancreas and injected into a diabetic dog tended to keep him free from sugar. He was making similar extracts for use in diabetic men when the world was electrified by a young Canadian doctor, E. G. Banting, who had made a very active extract from beef sweetbreads which he proved could be injected under the skin and would cause even severely ill diabetics to burn up their excess sugar, and would revive even those who were in the last stages of unconsciousness.

Since then, hundreds of thousands of diabetics lead comfortable and active lives, depending with confidence on daily injections of this substance, *insulin*, for their strength and comfort. They are not cured of the disease, but are able to prevent it from asserting itself by regular injections of the remedy. Just what this substance is, we do not know. Professor Abel, the great discoverer of epinephrine, has shown that it contains a compound of sulphur, and many sulphur compounds are active in the quiet oxidations that go on in chemical laboratories. He has obtained it in fine white crystals, and that is the first great step toward learning its exact composition, and then making it at will. What will be the next step we do not know. Much more work will have been done and many new substances tried out on animals, that the diabetic may know the complete comfort and safety that is sure to come with the remedies of the future.

Testing Drugs

Not only is experimentation on animals necessary for the discovery of new drugs, but the law requires that every sample of the old and well known drugs be tested on animals, to determine whether it is strong enough for its purpose, and safe enough to use on human beings. Every serum against diphtheria or lockjaw, every vaccine, every sample of insulin for diabetes, every sample of digitalis or aconite for heart disease must be thus tested.

Experiments upon animals have taught us the exact causes of most of the diseases that affect our health. It is only by such experiments that the remedies for (*Turn to next page*)

Legislative Season Ends

Medicine

A summary prepared by the American Association for Medical Progress.

Despite agitation by opponents of things as they are in matters medical, the state legislative season has closed with the legal status of medicine practically unchanged. Laws in certain states have been strengthened by restatement and by the addition of important clauses. None of the legislative blows made at the cause of medical progress achieved its purpose.

The most noteworthy legislation comes from Virginia, which state has incorporated its whole general body of medical law into one comprehensive act, covering registration of physicians, verification of licenses for practice, defining unprofessional conduct as a basis for revoking or refusing to grant licenses, providing the same high basic educational requirements for the practice of medicine, homeopathy, osteopathy or chiropractic, limiting the administering of drugs by unlicensed persons, and defining the status and rights of the chiropodist. Finally it defines the term "practicing medicine" as applied, and provides punishments in fine and imprisonment for violation of the law. The law also definitely prohibits the sharing of fees between a physician and a surgeon to whom the physician refers a patient.

In New York no less than sixty-seven bills dealing with various phases of medical practice were introduced in the Legislature. Only a few were ever reported out of committee. Those which did pass were largely in the nature of minor amendments and amplifications of existing regulations. The anti-vivisection bill in behalf of dogs, and the anti-vaccination bill both died in committee.

The Kentucky State Medical Board has again emerged unscathed from a particularly virulent legislative attack on its whole scope and organization. The "Ripper Bill", as it is known in the Blue Grass State, has appeared perennially for a long time. Adherents of the Board claim that this attack is purely political, and in general the Board of Health has had the backing of the medical profession and of the progressive element of the state.

In Washington, the Parker Bill, granting in general additional research facilities for the Public Health Service, passed but was vetoed.

Bills empowering the Smithsonian Institution to make recommendations for suitable recognition of research and other workers who risk life or health in the public service, and for granting pensions to the survivors of the yellow fever experiments, were reported out of the House committees before Congress adjourned. They will come up next winter.

Science News-Letter, July 21, 1928

Animal Experimentation—*Continued*

these diseases have been found and made safe and effective; and it is by experiments upon animals that the diseases for which specific remedies have not been found, will finally be conquered in the future.

Science News-Letter, July 21, 1928

Automobiles in New York City wreck $18,000 worth of lamp posts each year, and 60 per cent. of these accidents are due to intoxicated drivers.

Septic Sore Throat

Medicine

Septic sore throat, the disease that is responsible for the present large loss of life in the small Massachusetts village of Lee, is caused by a micro-organism very similar to the one causing scarlet fever. Both are members of the streptococcus family. They can only be differentiated by a complicated test which must be carried out on a human subject, officials of the U. S. Hygienic Laboratory said recently.

The present epidemic is by no means the first of the kind. Septic sore throat has occurred as an epidemic in this country and England since 1875. Generally the milk supply was the agent that spread the disease. In 1911 over a thousand cases with 38 deaths were reported in Boston, while Chicago, in the same year, had 10,000 cases within a few weeks. Baltimore had 3,000 cases with 30 deaths in 1912.

The milk becomes infected through the humans who handle it, and not through the cow, as in the case of tuberculosis. Cows may become infected with the organism, but it does not cause disease in them and such infection of the animal, as well as the contamination of the milk, is due to contact with infected humans, for this organism is not native to cows.

Science News-Letter, July 21, 1928

Magnetism and Static

Physics

When your radio crackles, squeals, moans, or stubbornly remains silent despite your coaxing, does the earth's magnetism have anything to do with such antics? That is what scientists of the Coast and Geodetic Survey have been trying to find out. F. P. Ulrich, magnetic observer of the Survey, stationed at Sitka, Alaska, summarizes the results of five years' observations by saying in a recent report: "In general, the condition of the earth's magnetic field is no index of the quality of radio reception." Thus the fact seems to be established that the earth's baffling magnetic forces are not to blame when your radio goes on a temperamental rampage.

Mr. Ulrich observed that the aurora borealis, or northern light, which is a manifestation of the earth's magnetism, occurs in greatest brilliancy on magnetically disturbed days. The aurora causes difficulties in cable transmission, he says, but "observations seem to indicate that good radio reception is very much more apt to occur than poor reception during a bright or faint aurora." That absolves the aurora, magnetism's magnificent advertisement, from suspicion of being the monkeywrench in radio's machinery.

In an effort to unravel the greatest of all scientific mysteries—the earth's magnetism—scientists have been making methodical, monotonous, deadly dull routine observations for years. They record the daily and hourly variations in the earths' magnetic forces at widely scattered observatories from Samoa to Honolulu and Alaska. An effort is also made to connect these records with other phenomena such as earthquakes, sun spots, and the aurora, and with radio reception and telegraphic and cable disturbances. It is hoped in this way to ferret out Nature's most profound secret—the secret of those magnetic forces which, up to now, have defied scientific analysis.

Science News-Letter, July 21, 1928

Among the world's needed inventions listed by British patentees are a collapsible umbrella to fit into a pocket; an unpuncturable pneumatic tire; rubberized fabric for heels, toes and soles of hosiery, and a clear name plate for streets that can be easily read by night or day.