

therefore, that Moir's and Dale's belief that a new highly important unidentified substance exists in ergot and its crude extracts (both aqueous and alcoholic), is confirmed by these studies. Quite contrary to their apparent belief, however, this new substance is shown to behave characteristically as an alkaloid, since the studies here reported show the presence of this new substance in the completely colorless "Total Alkaloidal Fraction," while the "Alkaloid-Free Fraction" proved to be devoid of any oral or subcutaneous activity of any significant type. The writer, therefore, believes that this new substance must be classified chemically as a new member of the "total specific alkaloids" of ergot, and that the activity of aqueous extracts, observed by Moir in human patients, is to be ascribed to "residual alkaloid."

(To be continued.)

ANTIDOTES. I. GENERAL PLAN.*

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Men from the earliest times have endeavored to find ways of relieving pain or injury to themselves by means of spirits, charms, mysticism, and later by use of herbs and animals. In these efforts they found some herbs and later extracts that were either beneficial or deadly. It was also observed that the animals were either beneficially or injuriously affected by certain plants or animals which they ate, as is reflected in the names—cowbane, sowbane and wolfbane which are plants poisonous to cattle, swine and wolves.

The fatal effects resulting from the bites of animals brought about the first real effort to find antidotes to poisons, though some earlier knowledge had been gained of the counter-action of one drug upon another. In Homer's "Iliad" describing the Trojan War and the adventures of ancient heroes (*Ca.* 1000 B.C.) many references are made to the wounds of the warriors being rubbed with a bitter, pain-assuaging root. Homer mentions 250 such cases. The earliest reference to a plant which was specifically believed to be an antidote for poison is found in Homer's "Odyssey;" "Moli" or "Molu" which is apparently a species of *Allium* (*Allium moly*). In this case Circe's potion was a form-transforming drug, the effects of which moly supposedly counteracted.

Among the earlier writers on antidotes was the Greek, Nicander of Colophon (185-135 B.C.), the Court Physician to Attalus, King of Pergamum, who made studies of poisons on condemned criminals, a common practice at that period. His first work, "Theriaca," which was written in Greek verse, had to do with the poisons of animal bite and treatments of them. His second poem, "Alexipharmaca," tells of antidotes to poisons. In these he mentions twenty-two poisons, including aconite, cantharides, opium and conium. His chief antidotes include warm oil, mallow and linseed tea to excite vomiting.

The development of antidotes to poisons was greatly stimulated when, about the time of Mithridates (first century B.C.), poisons began to be extensively used

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by certain ambitious or revengeful people to remove enemies or persons in the way of their personal advancement. The early effort was to develop a composite mixture of plant and animal materials that would protect against all poisons, bites of venomous animals and diseases. Several were put up in small cake or tablet form. A number of famous "theriaca," as the mixtures were called, were developed, containing from 37 to 250 ingredients guaranteeing protection. Mithridatium and two modifications of it were noted ones and appeared in the London Pharmacopœia as late as 1677 A.D. A red clay, "terra sigillata," which was excavated with much ceremony from a certain hill on the Island of Lemnos on August 6th of each year was given some attention. Tests in July 1580, showed that such a product saved the lives of dogs given lethal doses of mercury sublimate, aconite, apocynum or nerium! Subsequent reports of tests on condemned criminals, however, failed to show any more value for this product than for the unicorn's horn.

William Heberden (1710-1801) in his "Essay on Mithridatium and Theriaca" (1745) did much to expose the superstitions and worthlessness of these curious concoctions, and to banish them from the pharmacopœias. Antidotal studies since have been upon a more scientific basis.

A series of investigations have been made on various poisons by interested investigators. Some trials have been made on animals; some on humans. A great deal of information has been collected and has served as a basis for the preparation of various tables of antidotes. However, our search of the literature has failed to show any consistent study of several types of poisons under similar conditions. It was, therefore, deemed advisable to institute a detailed investigation along this line, with the hope of developing successful methods of treatment of men and animals.

Since the literature reveals enormous discrepancies in toxicity figures, we have repeated many determinations to establish authentic figures. Injections are given various laboratory animals, worms, fish, frogs, mice, rats, rabbits, cats and dogs by mouth, subcutaneously, intramuscularly, intraperitoneally or intravenously. We are also collecting recorded toxicological data for men.

Searches of the literature are being made to learn the suggested antidotes. Pharmacological and toxicological studies are made to serve as a rational basis for therapeutics. Based on this knowledge, the efficiency of various procedures for protecting against the fatal dose, and multiples of the fatal dose are being studied. Studies are being made of antidotal processes that may change the chemical nature of the poison, or prevent its absorption, or aid its elimination, or counteract its physiological effects, so as to save the life of a poisoned animal. In our present studies we are paying most attention to those poisons (strychnine, thallium, cyanides, arsenic and phosphorus), used in the control of noxious rodents and predatory animals.

CONCLUSIONS.

- (1) Detailed searches of the literature are being made to determine the lethal doses of various poisons for men and animals; also their antidotes.
 - (2) Laboratory studies are being made to learn the value of various procedures suggested in the literature or developed in our work.
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