

instinctive or emotional appeal subordinate reasons which, when the reader reflects upon his response, will provide him with a justification for that response.

Specifically, an appeal to a young mother in a sales letter to buy at a drug store strained vegetables for her infant may be based primarily upon the family love instinct. The letter should include in addition, however, a justification for the purchase, "Baby's health will be cared for. Care in infancy prevents many later ills."

Logical reasoning in sales letters is useful when action can be secured only after careful consideration. Generally it involves a choice of alternatives. Consider the problems involved in writing an effective letter which will convince a dispensing physician that he will serve his practice best and profit most if he writes prescriptions to be individually compounded by retail pharmacists rather than that he dispenses prepared medicines from his office.

Experienced druggists will see immediately in this and other like situations that logical reasoning should not be carried to the extreme of argument. Even when an argument is won, the reader of an argumentative sales letter feels that he has been forced unwillingly to an unwelcome conclusion. His attitude is one of grudging and crestfallen consent when it should be one of enthusiastic approval. The aim of every business letter should be to arouse a willing response.

BELLADONNA MONOGRAPHS.

BY FREDERICK B. KILMER.

(Continued from page 375, April number, *Jour. A. Ph. A.*)

DARIES' THESIS: "ATROPA BELLADONNA."

A notable landmark in the monographs devoted to Belladonna is one written by a Hamburg drug clerk, Peter John Andrew Daries, and published in 1776.

It was a graduation thesis submitted at the University of Leipzig, where he attained the degree of Doctor of Medicine.

This pamphlet monograph contains forty pages, and carries no illustrations. Not many copies are extant, and it is not generally referred to in the literature of the drug. The title page runs as follows:

"Concerning Atropa Belladonna
By The Authority Of The Most Gracious Order of Physicians
Under The Direction Of
Master Anthony William Plaz
Primarius Of Therapeutics, Dean Of The Medical
Faculty, Senior Member Of The National Saxon
Academy, Member Of The Board Of Gov-
ernors, 'Greater Chief' Colleague Of
The College, Member Of The Acad-
emy Of Natural Curiosities.

The Author, Peter John Andrew Daries, Bachelor Of Medicine,
Of Parchimo-Metropolitanus,
Will Dispute For The Degree Of Doctor. On August 30, 1776."

The thesis is written in Latin. While it bears evidence of careful study and preparation, its actual putting-together seems to have been hastily performed. Citations of authorities are numerous, but mainly those of the century in which the thesis was written. He did not search the ancient or classical writers.

Daries summarizes his thesis as follows:

"I will first give the various names of belladonna, next the botanical characters, then the constituted principles and official preparations, then the salutary and toxic effects will be expounded, and I will adhere chiefly to the powers of the roots, leaves, berries and seeds, with the additions which are discovered after death by autopsy. Then I may add what I, myself, have observed, and last of all will speak concerning the antidotes of belladonna."

In Daries' time the plant had become *Atropa belladonna*. He gives a very complete nomenclature of the drug, with citation of authorities for its use. His description of the plant is from personal observation. A list of countries in which the plant has been found is given. The use of the juice of the plant as a wrinkle remover and beautifier by the Italian women is noted.

Daries had obtained from the plant, by distillation, aromatic products with a yellow, oily, waxy residue and fixed salts. These constituents do not account for the peculiar powers of the plant. Poisonous plants, according to Daries, act "chiefly by a meandering vaporosity." This principle "gravolent and vaporous, infects and contaminates the fluids of the brain and parts of the nerves, suppresses their powers and stops vital action."

The curdling action of the juice of Belladonna upon milk seemed to Daries to typify its action upon the fluids of the body. If expressed in modern terms, Daries' explanation would be found to concur in part with our knowledge of the physiological action of the drug.

A fertile field for historical study lies in the section on "official preparations" which exhibits the author's training in pharmacy. He enumerates a score of preparations in use in his time in which the herb, the berries, the juice and the root are used.

Daries asserts all parts of the Belladonna plant are poisonous. He attempts to show that the power and effects produced by the root, leaf and berries vary from each other. This belief is still held by some of our present-day writers.

With Daries, as with many others, the poisonous power of the berries "smiling to the eye, but with poison in every drop of their luscious juice" is recorded. He notes that Belladonna is shunned by certain animals and by others eaten with impunity.

A sidelight on pharmacology of the past is noted in instances where Belladonna is injected into the stomach of animals in order that its effect may be observed. It took many centuries up to Daries to reach the conclusion that the power, the varying symptoms, and the results depended upon the amount of the drug injected, and that the action of the drug is influenced by age, sex, constitution and condition of the patient, and that some persons are tolerant to the point of immunity.

In a section devoted to "salutary effects" Daries breaks away from tradition and becomes at once an apologist and champion of Belladonna as possessing "worthy powers both in internal and external use."

He states that his century had been called the "toxophilic."

"I have especially read that belladonna is a poison, from the use of which any physician, no matter who, may prudently abstain (Blackwell).

"Lewis rejoices that it was abrogated by all authority.

"Hahn has said 'the question to be put is whether it is granted to an honest physician to use poisons?'

"But despite this reputation, I cannot see why I may not write of the very active poison and medicine—belladonna. Nothing seems to stand in the way of this, and I may have the good fortune to say something new concerning the effects of the drug."

This was, for the time, most presumptuous and unorthodox. The candidate for a degree was held to the citation of authorities recognized by the faculty. The candidate's own opinions and conclusions were to be rigidly barred from discussion. We may wonder how the thesis came to pass the conservative faculty of Leipzig.

Daries most heroically relates "experiments undertaken," and recites his epoch-making story.

"When a novice in the Hamburg pharmacy of my uncle, Orthman, Dr. Reimer desired some extract of belladonna. The fresh herb, with its flowers and fruit, having been finely comminuted, the better to boil out and extract the tincture, a bit of herb or drop of berry juice unfortunately splattered into my right eye.

"Realising this, I attempted in vain to remove the foreign irritant from the eye with the finger. Hardly had three minutes of the hour elapsed, the irritant action having ceased meanwhile, when a mistiness arose before the eye, which increased little by little. After quarter of an hour, there was present total blindness without any pain, the other eye remaining intact."

He sought the counsel of Dr. Reimer, the prescriber of the drug, and by proper treatment in three weeks his eye "was restored to its pristine integrity."

Reimer informed him that it was known that the ingestion of Belladonna would produce mydriasis, but he was surprised to learn that the external application of the drug would produce this result.

The discussion of the matter with Dr. Reimer resulted in the suggestion that this peculiar power of Belladonna might induce a harmless and temporary paralysis in the operation for cataract.

Through this the Hamburg drug clerk was stimulated to conduct a series of experiments upon animals.

His methods and results entitle him to a front rank as a pioneer in pharmacodynamics.

Quaintly he recites:

"If a cat or owl is placed in an utterly dark place, no light of any kind, and no light to appear, it is nevertheless reflected from the eyes, as soon as ever so little light is admitted.

"The eyes of these animals, before others, have the singular property that not only is the pupil much wider than the freer iris, and nowhere coherent to the cornea, but even the finest are pleased and moreover carry more also of aqueous humor between the cornea and crystalline humor, more remote from the pupil, but nearer to the retina, while endowed with non-pigmented choroid, and an obscure but pale flavescent or cerulean one. The conjunctival tunic of this cat, moistened with the juices of belladonna by means of a feather, one hour having hardly elapsed, the uvea became dilated, much more the right than the left, so that the chink was more than tenfold larger, and indeed assumed a circular shape, when formerly this had been oblong. In the eyes, moreover, nothing was seen of disease or cloudiness. Left to itself, the cat staggered as if drunk from the beginning, but a little later it walked with its accustomed gait, its head hanging, and tried with its fore feet to remove the application from its eyes.

"After an interval of two hours the phenomenon wholly disappeared, and the narrow longitudinal chink was restored to both eyes.

"With this experiment repeated with the dry herb in the right eye and the juice of the berry in the left, in a little while the uvea was dilated to the former circle. On the following morning the dilation of the pupil had again vanished. Therefore, instituting this experiment for the third time, the same result was obtained, but with this difference, that twelve hours having elapsed the pupils remained immobile.

"From this fact the cat was subjected to the anatomist's knife of my impartial friends, the distinguished Hebenstreit and Gerischer.

"In the alimentary canal, in the chest, abdomen and brain, no alterations were found. But on investigating the eye, the uvea, quite toward the wall of the sclerotic to which the choroid adheres, was flaccid and at the same time retracted in such manner that the pupil was tenfold larger than is found in the normal cat. The aqueous humor was clear, the vitreous indeed thin, almost watery, but nevertheless was quite soft.

"Likewise Rossi writes, 'dogs, cocks, chickens and small birds are disturbed by no sign of inflammation nor by pain, when their eyes are touched with a feather wet with the juice.' With two of the birds, a swallow and a lark, this experiment was carried out in the prescribed manner, and it is testified that this agrees perfectly with the truth, for the two birds developed no symptoms, the juice applied being gradually absorbed by the lacrymal points.

"These opinions, compared with the judgment of Dr. Reimer, concerning the application of belladonna as bound to induce a harmless temporary paralysis of the eye in order that extraction of the lens may be more readily carried out, seem to me to agree excellently."

Daries hastily concludes his monograph with this paragraph:

"Finished, therefore, is the copious discussion concerning the powers of belladonna, the salutary as well as the poisonous, which although possibly too lightly composed for a polished disputation, I submit to the judgment of the World of Letters."

We may well pause to pay due honor to this Hamburg drug clerk, Daries. His graduation thesis, now a "scrap of paper," adds much to the story of Belladonna. In it a condemned and rejected drug is restored to its rightful place in *materia medica*. What a loss to medicine and to mankind would have accrued if Belladonna and its narcotic congeners had remained under the ban which prevailed before Daries wrote his pamphlet. More than all, Daries opened the door which gave to the world a knowledge of the mydriatic action of Belladonna and other drugs of its class, a knowledge which conferred untold blessings upon mankind.

The world of letters, of medicine and of pharmacy—humanity itself—may well join in tribute to Peter John Andrew Daries.

BELLADONNA AFTER THE MONOGRAPHS.

The century following Daries, the last of the monographists, witnessed what might be termed a revolution in therapeutic practice, most notably the oncoming of organo-therapy, a sort of rebirth of the ancient animal therapy—physiotherapy—which was astrological medicine revamped.

In respect to the administration of drugs, many far-reaching changes occurred. A sceptical attitude arose in respect to the use of drugs in any form—a therapeutic nihilism and pessimism—and there was a strong battle against polypharmacy, which had prevailed in the previous centuries. The rise of homeopathy was a contributing factor in reducing dosage. Out of the conflict came a school which sought to study rationally and scientifically the action of drugs, old and new. In this turmoil, the solanaceous drugs, particularly Belladonna, have not only held their place, but advanced to new measures of usefulness.

More than forty years after Daries, another drug clerk, Runge (1810), had a similar experience to that of Daries in spattering the juice of Belladonna in his eye.

It started a train of thought that led to important results in the study of the mydriatic action of Belladonna and allied Solanums.

Runge, who is noted for his researches in the anilines, in consultation with the famous poet and scientist, Goethe, established the mydriatic action of other members of the solanaceous group. He separated what proved to be a mixture of the alkaloidal principles. This he called "Koromegen" (Greek—magnifier of the pupil). True Atropine was isolated in 1830 by the apothecary Mein; again independently in 1832 by Geiger and Hesse. Later, Leibig determined the chemical formula.

In the century following Sickels and Daries, we reach the time of multiplying literature. Belladonna and the mydriatic Solanums are treated systematically in books on materia medica, pharmacy, pharmacognosy and chemistry.

In the ever-increasing number of journals a mere list of titles of articles on these drugs, appearing in the period, would make up a portentous volume. An interesting feature of the medical literature lies in the vast amount of repetition. Many dissertations are found wherein the authors claim as a "discovery" of their own an action and use that had been noted hundreds of years before. Time and time again, writers issue a warning as to a "newly discovered" poisonous action of various parts of the Belladonna plant, the existence of which had been known for centuries. Extended, and at times acrimonious, has been the discussion as to the difference in action between the members of the related mydriatic plants and the various parts of the same plant. Hyoscyamus, Stramonium, Scopola and Belladonna have each had their advocates. The leaf, the herb and the root of Belladonna have been made official, and in turn deleted. Except in historical literature, the Mandrake has disappeared.

Full attention has been given to the use of the alkaloids in place of preparations from the plant, and likewise the shades of difference in the action of the different alkaloidal bodies. The methods of pharmacology have done much in the direction of clarification and simplification of the action of drugs, but in respect to Belladonna and like agents, the final test is at the bedside.

It was in the Nineteenth Century that real chemical methods were applied in the examination of Belladonna. In the first decade of the century, Louis Nicholas Vauquelin, an apothecary and director of the School of Pharmacy at Paris, is credited with the first proximate analysis. During the years that followed, a rather formidable list of substances have been laid down as having been found in Belladonna. Here are some of them:

Starch, sugars, honey and saccharates, cellulose, gums, wax, resins, mucilages, asparagine, albumin.

Coloring Matters: Chlorophyl, anthocyanin purple, xanthophyll yellow, atrosin.

Alkaloids: Atropine, hyoscyamine, belladonine, atropamine, apatropine.

Acids: Acetic, malic, chrysatropic, succinic, prendatorin, phyteumscolla.

Salts: Potassium sulphate, nitrate, phosphate, chloride, hydrochlorate, oxalate, malate; magnesium malate, phosphate; sodium chloride, phosphate; calcium malate, oxalate; ammonium salts.

Odoriferous and aromatic principles.

We cannot presume that all of the substances named in this array exist as such in Belladonna. Some of them no doubt are formed during the chemical manipulations

of the drug. But as they stand, they constitute our chemical knowledge of Belladonna, gained during the years following the monographs up to now.

In the pharmacy of the mydriatic group, much has been done upon processes of assay, upon the pharmacognosy, upon standardizing the actions of the drugs and upon methods of extraction. Except for the preparations of the alkaloids, pharmaceutical compounds have not changed materially since the time of the monographs. Notable is the fact that alcoholic extractions and preparations from fresh juice—the green extracts of the Continent—have persisted. Writers have repeatedly urged the need for improvement in the preparations of the mydriatic, as well as other vegetable drugs.

The cultivation of drug plants, including those in the mydriatic group, runs through all centuries. In the period following the one we are reviewing, advanced cultivation methods were applied to Belladonna, Hyoscyamus and Stramonium. This was stimulated by the increased use of the drugs, which caused a shortage of supply. The literature is filled with discussions as to the respective medicinal value of the wild and the cultivated drug. In the cultivation of Belladonna and Hyoscyamus, difficulties, which have not yet been mastered, were encountered, since these particular plants were greatly influenced by any change in their environment. As in previous centuries, the main source of supply for the mydriatic drugs in all countries remains in the hands of herb gatherers. This in itself prevents uniformity in methods of gathering and in conservation, and hence a variation in quality.

The literature of the Nineteenth Century is filled with discussions of pharmacopœial and legal standards and regulations for the control of the quality of Belladonna and the mydriatic Solanums. Nature has her own standards, which man cannot change. Neither pharmacopœias nor market regulations can control peasant gatherers in the mountain fastnesses. When the pharmacopœias based the standard of pharmacopœial preparations of the mydriatic drugs upon the alkaloidal content, commerce fixed the value of the drug upon a like basis. This was a sane and progressive step toward uniformity.

Notable in the Nineteenth Century was the growth of scientific medicine, the revival and extension of experimental investigation, the establishment of research laboratories—physiological, pharmacological, biological and chemical; the growth of specialism, advancement of diagnosis, the progress in medical education; the rise of preventive medicine on the foundations of bacteriology. The century includes the discovery of anæsthesia, Roentgen-rays and the entrance of surgery into the "Modern Era."

Osler tersely summarizes the Nineteenth Century as a period wherein

"Science emptied upon man from the horn of *Almalthea* blessings which cannot be enumerated, blessings which have made the century forever memorable, and which have followed each other with a rapidity so bewildering that we know not what to expect next. The great boon of this wonderful century, with which no other can be compared, has been the fact that the leaves of the tree of science have been used for the healing of the nations. This is the Promethean gift of the century to man."

Through the revolutions and kaleidoscopic changes in medical practice, Belladonna and its congeners have retained their place in therapy. The separation of the alkaloids, to a degree, changed the form of administration and increased

the use of these drugs. At the end of the first quarter of the Twentieth Century, a writer (Sajous) frankly states that the many therapeutic properties that had been credited to Belladonna have been sustained by modern research. It holds a more exalted position than ever before in the history of medicine. In part, this has been due to the growth of scientific pharmacology, and in another part to the achievement of discovering the "vital principles" of the ancients—the alkaloids of modern pharmacy.

The three monographs here outlined consist of a few "leaves" from the history of Belladonna, covering, in part, two centuries and carrying it toward the opening of the Nineteenth. Each of the writers made material additions to the knowledge of Belladonna. Faber classified and systematized the records which had been put down and added his own far-reaching observations. Sickels gave a view of the drug as it appeared in his own age. Daries, through original research, opened the door which led to the production of the alkaloidal principles which have proven of such great value to mankind. To these three writers we may well accord due honor.

A modern writer has stated that "in respect to Belladonna, much has been written, much forgotten, but about it really little is known." What the future may have in store cannot be foretold. There is nothing to indicate that the usefulness of Belladonna and allied drugs will not continue. More than ever before, their place is firmly fixed among the most important drugs in our *materia medica*, and they are well worthy of the studious labor that has been bestowed upon them.

THE NEW MEDICINAL PLANT AND VOLATILE OIL PRODUCTION
LABORATORY OF THE DIVISION OF DRUG AND RELATED PLANTS,
U. S. DEPARTMENT OF AGRICULTURE.

BY A. F. SIEVERS.

The Division of Drug and Related Plants of the Bureau of Plant Industry, U. S. Department of Agriculture, has for many years conducted investigations on the production of plants yielding medicinal products and volatile and fixed oils at the Department's experiment farm near Rosslyn, Va., across the river from Washington, D. C. The main objective of these investigations has been to determine the cultural requirements of such plants and to study the quantity and quality of their products, with special consideration to the possibilities of such plants as commercial crops in this country. In the prosecution of this work it is necessary to maintain a laboratory at the farm to handle the crops produced in connection with the field experiments, including the drying of seed and herb, the grinding of the herb, the distillation of the volatile oils, and various other operations that are usually associated with such investigations.

The organization of this work began in 1902, but it was not until 1907 that it was permanently located on the Department farm in approximately its present location. A lath structure for partial shade was provided and numerous species of medicinal interest were placed under cultivation. About six years later a permanent exhibition garden with 39 beds was laid out and this has been maintained without interruption up to the present time. In recent years an area of approximately two acres has been devoted to the cultural experiments. Some plants that show par-