

In many cases such studies can be carried out on normal individuals, and within a short space of time sufficient data can be accumulated to establish with scientific accuracy certain aspects of drug action.

Ultimately, however, we must answer the question: Are these drug effects of value in combating the disturbances of functions that are encountered in disease? The final answer to this question can seldom if ever be given from studies either on normal animals or on normal men. In certain instances the diseased function is unusually susceptible to drug action. The body temperature of a febrile patient, for example, is reduced more easily by antipyretic drugs than is the body temperature of a normal person. Digitalis in therapeutic doses has relatively little effect on the heart rate when this is controlled in the usual way from the sinus region. Its reputation for slowing the heart of patients is based almost exclusively on observations which were made on those suffering from auricular fibrillation. Diuretics of the caffeine group produce a moderate diuresis in the healthy man, and may be ineffective or harmful in nephritic edema, whereas in cardiac edema they often cause a veritable flood of urine. The dilatation of the bronchi produced by epinephrin is most plainly demonstrable in conditions of bronchial constriction, whether produced experimentally or occurring during asthma. Finally, the treatment of infections can manifestly be tested only on infected animals or human beings.

Not infrequently the remark is made that the value of a therapeutic measure is determined solely by clinical experience. While I have no desire to contradict this assertion, it should be pointed out that ordinary clinical observations are often extremely difficult to interpret, owing to the vagaries of disease and to the many remedies that are so commonly employed in a single case. The past history of therapeutics warns us that in order to avoid error we need as much assistance as possible from every source. Pharmacology may not, indeed, answer therapeutic problems directly, but at least it aids in their solution. It shows how drug action may be made the subject of accurate study, and the critical attitude which it adopts must be carried over into the interpretation of therapeutic results, if progress in that subject is to be placed on a firm foundation.

On the other hand, pharmacologists could, I believe, be of greater help to those who work in the clinic if they would fully realize how their results may be given a form more suited to clinical needs. What, for example, is the effect of a given drug in small doses, especially when given over a long period of time? How are the effects modified when animals have been made the subject of disease? What pharmacologic problems can be studied on man himself, and especially on patients who are taking the treatment usually given for their disease? Work on such lines as these, whether by pharmacologists or by clinicians, will help to maintain contact between the science of drug action and the art of treatment.

CRITICISMS AND COMMENTS ON THE NATIONAL FORMULARY IV.*

BY JACOB DINER.

In the early days of the Formulary it represented a collection of formulae, gathered more or less indiscriminately from all corners, and endeavoring, in a most laudable manner, to unify, as far as possible, the rather divergent composi-

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tions and constituents of preparations of the same name. The book was more in the nature of a reference book, was not official and therefore compliance with its formulae was neither binding on the compounder nor was deviation from formula a violation of and punishable by law. The conception as well as the execution of this book was most commendable and the originators as well as all subsequent workers and revisers deserve the highest commendation from the body pharmaceutical as well as from the members of the medical profession. However, two events have made it essential that this book should not only be a good reference book but that it be the best of its kind, and that it should be scientific and rational to the smallest minutiae. These two events are: Firstly, the passage of the National Pure Food and Drug Act, making the N. F. an official book of standards, and secondly, the ever increasing propaganda for legitimate and rational prescribing. To this may be added a third reason or consideration for care in the compiling and revising of the Formulary.

America and Americans have lived in a land where "milk and honey flowed." The "Horn of Plenty" was pouring out its contents in a seemingly never ending stream and the thought of conservation never entered our mind. The events of the past two years have brought home to us the meaning of the word "Conservation," and it is the duty of every good American individually and collectively to acquire the habit of Conserving and take a few lessons in Thrift. This has been done in the thorough American way with regard to money, food and clothing, and it behooves us to do likewise in the matter of drugs.

I do not by any means wish to advocate the saving of drugs at the sacrifice of health or life, but I do wish to emphasize that many drugs, which have been used lavishly because they were abundant, could well be eliminated or used more sparingly because they are not essential in the treatment of disease, and are badly needed for other important purposes.

Viewing the revision of the National Formulary from these three points we can divide my criticism of some of the N. F. preparations into three classes:

1. Non-essential preparations. By that I mean preparations which merely increase the bulk of the volume, adding neither to "elegant" pharmacy nor to the knowledge and armamentarium of the practitioner of medicine. Among these I might mention such preparations as Acetum Aromaticum and Aqua Phenolata. The first of these, at best, is but a useless toilet preparation hardly known to and rarely employed by either public, pharmacist or physician. The latter merely a 2 percent (approximately) solution of phenol, rarely used in that strength and easily made extemporaneously. Both of these and similar preparations merely clutter up the book, adding to its volume but not to its value.

2. Unscientific preparations. These can be divided into two classes: (a) Physiologically incompatible. A very good example of these is furnished by the different elixirs of the bromides.

Albertoni found that bromides lower the excitability of the motor cortex of dogs, so that a stimulation of the motor areas which under the conditions of the experiment gives rise to general epileptiform convulsions, will, after the administration of a bromide, be confined to the area directly stimulated.

Walter A. Bastedo states with reference to Bromides: "On the whole central nervous system except the medulla, there is a moderate but lasting general depression. Bromides have their chief employment as sedatives."

Potter says: "The Bromides are powerful depressants to the nervous system—they lower the activity of the cortical motor area and that of the brain as a whole, * * * * they lower the reflex excitability of the spinal cord," etc.

Stevens, A. A.: "Bromides are used to control convulsions, to allay nervous excitement," etc. Many more authors could be cited; but it requires no quotations to establish the fact that bromides are used as sedatives and anti-convulsants.

Now let us look at the action of alcohol when given in small doses. Quoting from the same authors, we find Sollmann's statement as to the "Stimulant Effects of Alcohol" as follows: These are observed in most individuals after taking "moderate" doses of alcohol. The phenomena are only too well known. There is an increase in the rate of the respiration and of the heart; the blood pressure rises. *There is an increased vivacity of motion, action, and speech.* * * * *

Bastedo, under Alcohol, these (highest faculties) are depressed and there is a certain degree of freedom from restraint, *i. e.*, "there is a breaking of the fetters which keep our animal natures within bounds."

Potter states, "that * * by a moderate dose this entire system (nervous system) is briefly stimulated" * * and again: "Internally in moderate quantity a single dose of alcohol acts briefly as a cerebral, cardiac and general stimulant."

Stevens maintains, "that alcohol first stimulates and then paralyzes all parts of the nervous system."

Personally I have no particular grudge against alcohol. I am neither an advocate of total prohibition, nor do I maintain that alcohol is entirely useless pharmacologically. Neither do I believe in the indiscriminate use of alcohol, especially so when it is given disguised, as in the case of elixirs, and where the "well feeling" so frequently noticed immediately after partaking of alcoholic beverages may lead the patient to an ever and ever increasing use of the drug. I believe, with many other pharmacologists, that alcohol is a depressant to the higher centers. I am in the habit of telling the students that the old-fashioned saying, "alcohol loosens the tongue" is a very accurate and scientific observation. The sense of deliberation and control is gone and, "the impulse rather than the sense rules." Now if we are going to employ bromides for the purpose of allaying hyperexcitability, a condition most decidedly akin to, if not entirely due to loss of control by higher centers, why combine it with a drug which principally acts as a depressant to the higher centers and has indirectly, if not directly, a stimulant effect upon our reflexes.

The only possible excuse that can be made in favor of the elixirs of bromides is that of palatability. But this is not founded on facts. We can present bromides in much more palatable form by the aid of syrup to which a small amount of citric acid is added or by the use of a fruit syrup, especially pineapple syrup.

(b) Irrational formulae, good examples of which are furnished by the different liquid preparations of bismuth salts. Of these salts pharmacologists state as follows:

Cushny: "Bismuth acts simply as a protective *powder* with perhaps some astringent properties. It has been found that when swallowed it is at first deposited in the most dependant part of the stomach, but is later distributed evenly over

the surface and forms a continuous sheet over any ulceration, which it thus protects from mechanical injury from the food and also from the chemical action of the gastric juice."

Sollmann states: "The *insoluble* basic bismuth salts are used on inflamed surfaces. They act largely mechanically."

Potter maintains, "that the action of the insoluble bismuth salts is chiefly a local one."

Stevens describes the action as feebly astringent and protective and Bastedo concurs in that view, and adds, "that internally the insoluble bismuth salts are used."

We know from experiments, both in men and animals, that absorption of bismuth salts causes a marked cardiac depression and may lead to other toxic symptoms. Admitting even that the hydrochloric acid of the stomach will precipitate the soluble bismuth salt from its solution, why should we bring it into solution first only to have it precipitated again? Surely the claim of palatability could not be made in favor of the bismuth solutions because bismuth salts are not at all disagreeable to the taste. Why then have a number of bismuth solutions such as Elixir Bismuthi, Elixir Cinchonæ Alkaloidorum, Ferri, Bismuthi et Strychninæ, and many others.

Another class of irrational formulæ is represented by the alcoholic diuretics. We know that alcohol is an irritant to the renal epithelium and we also know that constant irritation of the kidney by alcohol leads to degenerative changes. What then can be accomplished, in a remedial way, by such preparations as Elixir Buchu with its many variations contained in the N. F.? Is it wise to break away from the old maxim: "Do no harm if you cannot do good."

Lastly, what is the object of the very numerous elixirs of cinchona and cinchona alkaloids? And equally insistent is the question why should we have such a varying dose of strychnine? In the Elixir Cinchonæ Alkaloidorum, Ferri, Bismuthi et Strychninæ we have 0.7 mg. of strychnine sulphate per 4 Cc. dose, similarly in the Elixir Cinchonæ Alkaloidorum, Ferri et Strychninæ, and in the Elixir Ferri Quininæ et Strychninæ. In the Elixir Ferri Pyrophosphatis, Quininæ et Strychninæ we have 0.56 mg. strychnine alkaloid for 4 Cc. dose while in the Elixir Pepsini, Bismuthi et Strychninæ we have 0.7 mg. of the alkaloid and in Elixir Glycerophosphatum Compositum only 0.5 mg. of strychnine glycerophosphate is given in each 4 Cc., but 8 Cc. is recommended as an average dose. I know that my critics will bring up the fact of atomic weight as explanation of the difference in doses. But against this I will say, that cannot explain the difference between the doses of 0.7 mg., 0.56 mg. and 0.5 mg. of strychnine alkaloid. Furthermore, in none of these preparations a very large dose of strychnine is given—would it not be more logical to have all preparations of strychnine and strychnine salts of the same strength, so that the physician could more readily remember how much strychnine he is prescribing?

In conclusion, I want to emphasize the fact that if we would have the physician make use of the National Formulary it behooves us to reduce its volume, simplify and standardize its formulæ, and make the book scientifically unassailable.

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- Walter A Bastedo, "Materia Medica, Pharmacology and Therapeutics."
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DISCUSSION.

W. L. SCOVILLE: This is the first constructive criticism I have heard on the National Formulary, and it is helpful. The arguments are logical, but unfortunately human nature is not logical, and that is where the difficulty lies. I would like to state a few facts about the National Formulary as a matter of interest. Not in criticism of the paper, because I have none, but there are always two sides to a question. Doctor Diner has criticized the therapeutic action and justly so. In the early stages of the last revision the Formulary Committee made a special effort to obviate just that sort of criticism, and get the therapeutic questions settled. To do so they invited coöperation on the part of the medical societies. The American Medical Association appointed a committee to coöperate with the National Formulary Committee. We had a meeting, and the American Medical men simply said, "You must drop this and that; you must not do this and that." "What can we do?" we asked, and they replied, "Of course it is up to you; you must do so and so." We tried to reason with them, but did not come to an agreement. They were using those preparations and calling for them, and we asked if they did not want them standardized, and the answer was "No, we can not stand for that." Anyway, it came to a stage where we said we did not see how we could coöperate. We parted good friends, but simply had to take the situation as the pharmacists saw it, and did not further attempt to settle the question. The National Formulary Committee can not settle it unless the medical profession can come to a closer agreement.

LIQUOR CRESOLIS COMPOSITUS, U. S. P. IX.*

SUBSTITUTION OF OTHER OILS INSTEAD OF LINSEED OIL IN THIS FORMULA.

BY WILLIAM W. DAVIES.¹

Our Allies across the seas, and our enemies as well, have found it expedient and necessary in many instances to revise their pharmaceutical formulae to meet the conditions brought about by these war-times. Many of our large medicinal manufacturers have likewise gone over their private and special formulae and made changes which as perfectly well result in the desired therapeutic action of their products. Again it has been suggested from time to time that the Pharmacopoeial Committee should likewise heed the trend of affairs and permit certain variations in their set formulae in accordance with the apparent demand of the times. It may be here stated that the Pharmacopoeial Committee really has already done this very thing as we may note for instance in the formulae of *Liquor Cresolis Compositus* and *Pilulae Ferri Carbonatis* (Blaud's Pills) where the potassium salt used may be replaced by the equivalent amount of the cheaper sodium salt.

For the same reason of economy and conservation of supplies, it is the object of this paper to call attention to the desirability of permitting the substitution of Linseed Oil by the proper proportion of other cheaper oils, such as Soya Bean Oil or the like. This substitution will not change the germicidal value of the product since the percent of Cresol would remain the same.

The demand for Linseed Oil in the trades has caused the Government only recently to issue a request for the conservation of its supply. In this particular

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