SUBSTITUTIONS, ITS EVILS AND NEED OF BETTER CONTROL.*

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The efficacy of medication depends in a very large measure upon the pharmacist's dispensing exactly what the doctor orders. Physicians come nearest the sick and are best qualified by education, training and experience, to decide what medication is best suited for their patients. Every honest pharmacist is opposed to the rascally business of substitution but still it goes on and on. Tampering with prescriptions is a serious proposition. In order to accomplish the greatest good for the suffering sick there must be complete harmony and coördination between the professions of Medicine and Pharmacy. It is sad to relate, but true, that substitution in Pharmacy has caused marked trouble down through the ages. I have met with plenty of it during the past forty years. I well recall, during the eighteen-nineties, the unpleasantness that resulted from the exposure and practical ruin of a prominent druggist in Philadelphia, for substituting in the filling of doctors' prescriptions. The leading instances of substitution and adulteration led to the all-inclusive drug definition in the National Food and Drug Law.

In the Report of the New York City Health Department, January 10, 1903, it is stated that 320 out of 373 samples of a drug purchased in drug stores were either gross substitutions or rank adulterations. These reported alleged adulterations were in truth largely just plain substitutions. The Food and Drug bills under active consideration by Congress, at the time, covered United States Pharmacopœial drugs only, a compromise satisfactory to but a few. Certain drug interests vigorously protested the limiting of drugs to be covered by a National law and requested a hearing on the subject, which was granted. At this hearing the glaring substitutions and adulterations reported by New York City Health Department and others were prominently featured. The drug representatives declared that the above limitations would preclude reaching thousands of substitutions and adulterations and would raise havoc with the filling of physician's prescriptions and the suffering sick. The hearing resulted in the following addition to the drug definition: "Also any substance intended to be used for the cure, mitigation and prevention of disease."

The amplified drug definition was included in a later Senate Food and Drug bill which caused a great rift in the various branches of the pharmaceutical profession. Strange as it may seem determined efforts were then made by the drug trade to prevent favorable action thereon by Congress, and Senator W. B. Heyburn, chairman of the Committee having charge of the bill, and other Senators were as determined to retain the enlarged definition. The bill failed to pass in the Senate, it was claimed largely because of the opposition to the amplification of the drug definition by the drug trade. Senator Heyburn was personally blamed for this failure, because he stubbornly and foolishly insisted on retaining the omnibus drug definition.

Senator Heyburn asserted that if the bill failed of passage he would introduce a like bill in the next, the 59th Congress. He made good his assertion. The bill

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contained the same offensive drug definition. Congressman Wm. P. Hepburn introduced a like bill in the House, without the inclusive drug definition. The contest was on and it was a bitter one. The bill passed the Senate with the enlarged drug definition, was finally accepted by the House and ultimately became a part of the National Food and Drugs Act, June 30, 1906.

A more extensive summary of this struggle, by the author, is contained in an article on "Physicians' Prescriptions" which will be published in a later issue of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Notwithstanding the fact that substitution played such a prominent part in the development and inclusion of the omnibus drug definition in the national law, the term substitution is not found in the act. It was possibly assumed that adulteration or misbranding, or both, covered substitution, but there are marked differences between substitution, adulteration and misbranding, as applied to drugs.

During the past year I came across an article on the old-time evil, written by O. U. Sisson, an eminent pharmacist, which both surprised and grieved me. It surprised me because of such an apparent prevalence of substitution in some places and grieved me because it reflects unfairly on some of my good apothecary friends in addition to giving the all-too-eager reporters the opportunity to speak reproachfully about the profession of Pharmacy. This occurred in a state which has had an anti-substitution law on its statute books for over thirty years. Said he, "So much has recently appeared in print regarding substitution in drug stores. Substitution literally means the giving of something of a lesser standard in place of the one prescribed or called for. No one having professional ethics at heart, can honestly condone or tolerate substitution in any form or nature in the dispensing of drugs, whether these be requested by physicians' prescriptions or otherwise."

He further calls attention to the fact that most of the alleged substitutions found during the Chicago hearings of the State Department of Registration and Education of the State of Illinois consisted in the dispensing of preparations of manufacturers other than the ones designated by the prescribing physicians. He does not consider this practice as objectionable as the substitution of a lower standard for the one called for. In the filling of prescriptions the only standard is the prescription. Substitution is substitution irrespective of any standard aside from the prescription itself. No one is justified in making any changes in any prescription without the advice and the consent of the physician. Otherwise the physician's objective may be thwarted. It is indeed morally if not legally wrong, and if the present laws or their enforcement do not reach the evil, the better element of the pharmaceutical profession should rectify the situation. If this is not done I venture the prediction that some outside agency will do the work for them. In fact, some of this has already been done and more can be expected in time.

In a private communication to me Druggist Sisson says, "This particular article was inspired because of the tirade carried on by the State Department of Registration and Education, in which many were accused. There were quite a few convictions and others were released for lack of evidence." Our friend makes the error, so frequently made by others, of criticizing or even reviling officers of the law, for doing their sworn duty in the enforcement of laws committed to their charge. It is a well-established axiom that laws will not enforce themselves and it is self-evident that enforcing any worth-while law will hurt some one.

State anti-adulteration laws made their appearance a century ago and later, but apparently no special efforts were made to enforce them, until those of the eighties were enacted. Those of us whose memories go back that far recall the abuse and calumny heaped on some of the state officials who enforced these laws as they saw them, without fear or favor. Those whose memories do not go back far enough can read with profit the records of the hectic activities in these fields. As to how well these laws have been enforced I have no definite knowledge, but it does seem that if they had been enforced in the spirit in which they were enacted there would be less substitution than seems to prevail at present.

Studies on the Qualities of Drugs in the District of Columbia and Court Decisions on Prescription Filling under the National Law.—Samples of standard drugs such as tincture of iodine, solution of citrate of magnesia, paregoric, soap liniment, elixir of iron, quinine and strychnine, tannic acid ointment, chloroform liniment, aromatic spirits of ammonia and others were purchased from time to time and tested as to purity and strength. The study was primarily made to ascertain the character of the medicines vended and possibly furnished on prescription. In cases where deviations from the standards were considerable, the vendors were either advised concerning the shortcomings or cited for hearings. The work was essentially educational. Some of the samples purchased later and found to vary unduly from the standards (2) were referred for court action. None of these cases was contested. A few of the cases passed on by the courts (3) and their defects are noted herewith; tincture of iodine, deficient in iodine and without potassium iodide; tincture of iodine, one-third standard strength in both iodine and potassium iodide; paregoric, one-third amount of opium required; soap liniment, methyl alcohol substituted in part for ethyl alcohol.

Complaints and criticisms were received at intervals about laxity and substitution in the filling of prescriptions. This was considered a part of the duties of the District Officials, but in time this line of work received some attention by the Bureau of Chemistry. The results (4) on the whole were fairly good, but in a few cases manifest carelessness existed and some substitution was disclosed. It was fully realized that this line of investigation reached into a new field and required the exercise of care. It was therefore decided to ascertain the cause or causes and, if possible, to help remedy the defects. No reasonable excuses were offered for the substitutions and, as noted above, the law does not specifically cover substitution. After weighing all of the evidence and the conditions obtaining, it was decided to take representative cases into Court. The Court passed on (5) and imposed modest fines in the following cases: substituting bismuth subcarbonate for bismuth subnitrate; antipyrin for acetphenetidin, and, in a third case, for short weights of two chemicals called for in the prescription.

There then appears to have been a period of quiescence in this line of work. At least neither of the indexes of the Notices of Judgments record any cases in the field of physicians' prescriptions. In November 1931 the Food and Drug Administration had about one hundred physicians' prescriptions filled by pharmacists in the District of Columbia. An examination of the products dispensed showed that some fifteen were sufficiently adulterated to cite the dispensers for prosecution. All but one of the druggists charged with violating the law entered pleas of guilty. The Court in some cases ordered that the imposition of a sentence be suspended, and each of the rest received a suspended sentence of twenty-five dollars. The case of the druggist who resisted the charge of adulteration had a decidedly different termination. After hearing the evidence the judge took the case under advisement and later in dismissing it ruled as follows: (6) "Inasmuch as the Government did not comply with the regulations made pursuant to the Act in regard to the procedure, it occurs to the Court that the same strict construction should apply to the Government as is contemplated against the defendant, and the case is accordingly dismissed." This is certainly a pretty severe indictment. The chief reason for this ruling was a failure to give the defendant a portion of the sample dispensed by the pharmacist.

Later, additional samples were collected on prescriptions by the Administration. Of these forty-two found their way into Court. It appears that the defendants tentatively agreed among themselves to abide by whatever decision might be rendered in any one case. The charge in the case tried was, briefly, that the compounded prescription fell below the professed standard under

which it was sold, because it should have contained 3 grs. of codeine sulfate, but in fact contained not less than 3.7 grs. of codeine sulfate. Indeed it actually fell above the standard instead of below it. The law does not specifically make it an offense to sell a drug above the professed standard. This charge therefore read something into the law that is not there, but the defendant could not very well raise this issue, because it involved a narcotic drug. On the whole it was not a very good case to try out an important issue. The case was actually tried out on demurrers. The Court sustained the demurrers, of which there were seven. The leading one in my opinion is the following: "That the Food and Drugs Act of June 30, 1906, does not apply to prescriptions compounded by a pharmacist" (7).

The above are certainly two vital decisions and if allowed to stand, the law to which they apply is practically inoperative, as far as concerns the dispensing of prescriptions, by pharmacists. Furthermore there seems to be little enthusiasm in either appealing the cases or bringing or prosecuting new cases. As things now stand there appears to be little specific legislation in the District controlling the filling of prescriptions, except in the case of certain narcotic drugs. It may be that something can be done under the District of Columbia Food and Drugs Act of 1898, but diligent search fails to disclose any action ever having been taken to deal with substitution in the case of physicians' prescriptions. A reading of the new Food, Drug and Cosmetic Act of June 25, 1938, does not seem to give any help on substitution problems.

According to the information communicated to me, all of the preparations covered by Notices of Judgments Nos. 26106 to 26116, inclusive, published in 1937, were purchased on physicians' prescriptions. A study of these documents fails to disclose that any of them were so purchased. This to my mind is omitting an important feature, particularly in view of the latter court decision, quoted above. The fact that they were purchased on physicians' prescriptons should be noted in the records published by direction of Congress. In the Notices of Judgment Nos. 5019, 5615 and 5622, published in 1918, dealing with the filling of physicians' prescriptions, this information is clearly set forth in the title of each case and is noted in the indexes. Any one desiring information on this point, in the later cases, will be compelled to look somewhere back of the published records, which in most instances is impractical.

In the above three Notices of Judgments, published in 1918, physicians' prescriptions are recognized as standards, in similar language of which the following is representative: "That its strength and purity fell below the professed standard and quality under which it was sold—." Similar language is contained in Notices of Judgments Nos. 26106 to 26116, inclusive, published in 1937, thus again recognizing physicians' prescriptions as standards. Prescriptions have from time immemorial been considered tacit standards, but these are the first instances in which they are definitely recognized as such in Government publications, issued by mandate of Congress.

Representative W. H. F. Lee was the first to use the term "misbranded" in Federal Food and Drug legislation. It appears several times in his comprehensive bill, introduced in Congress June 4, 1888. From this time on it retained a place in this type of bill and was finally made a part of the national law. Since then it has been utilized to meet various alleged violations, never intended originally. Modern dictionaries define the word "misbrand" briefly, to label or brand improperly or falsely. The definition in the law is much broader, but it is doubtful if much of it is applicable in cases of substitution in the filling of prescriptions, for the simple reason that aside from the parties immediately concerned, there is nothing on the label of the filled prescription excepting directions for its use.

There were two cases of substitution, Notices of Judgment Nos. 5019 and 5615, tried in the Court on the charge of misbranding. It must be admitted that this charge was far-fetched. There was no contest. These offenders had no standing in Court, but it is not good policy to bring action in a case of this character. It raises a question as to fairness of the enforcing officials. In the 1934 New York law, substitution and misbranding are defined in the same sentence. This may be helpful.

Anti-Substitution Laws in Some of the States and Territories.—There is definite evidence of record that substitution in the dispensing of prescriptions and otherwise is on a somewhat different footing than either adulteration or misbranding. Indeed there are some special laws on the subject, showing marked differences. Bulletin No. 98, revised, of the Bureau of Chemistry, 1908, contains some of the then-existing ones (8), namely: Arizona, Idaho, Illinois, Mary-

land, New York, Porto Rico and Tennessee. An effort will be made here to give brief extracts of these and other anti-substitution laws.

Controlling substitution in the filling of prescriptions in New York State, had its origin in 1864 (9), with a Commission appointed to codify the laws of the State. The Commission proposed the draft in pursuance of the frequent occurrence of accidents, even resulting in the loss of life, through mistakes in the putting up of prescriptions. Reference is made to a court case in which extract of belladonna was used in the filling of a prescription, in place of extract of dandelion, resulting in a dangerous illness. The proposed draft of the Commission was enacted into law in 1881 (10), and reads in part: "An apothecary, or druggist or any person employed as a clerk or salesman by an apothecary or druggist, who in making up any prescription or filling any order for drugs or medicines, willfully, negligently or ignorantly substitutes a different article than that prescribed or ordered, in consequence of which human life or health is endangered, is guilty of a misdemeanor." This phraseology certainly leaves ample opportunity for a clever substituter to substitute without fear of committing an offense. It should be noted that some of the laws enacted later on this subject contain a similar endangering proviso.

The same year, 1881, the New York State legislature enacted a so-called modern food and drug law (11) which shows that substitution and adulteration were even considered different evils and must be handled differently.

Both of these laws, materially amended, are retained to the present time. The anti-substitution act as amended in 1907 (12) forbids any person putting up a drug, medicine, food or preparation, or substituting or dispensing a different article from that prescribed or ordered, or in any way deviating from the terms of the prescription. He is at liberty, except in the case of prescriptions, to recommend the purchase of another article than the one called for or ordered, but it must be of a similar nature, with the full knowledge of the purchaser.

A conviction under this law is punishable as a misdemeanor. For a second conviction the offender must be sentenced to imprisonment for a term of not less than ten days nor more than one year, and to the payment of a fine of not less than ten dollars nor more than five hundred dollars. For a third conviction he is not only liable for the above penalties but "shall forfeit any right which he may possess under the laws of this State at the time of such connection to engage in any capacity in the compounding, preparing or dispensing medical prescriptions or orders for drugs, medicines or foods or preparations used in the medical practice." This drastic act, so different from the early one of 1881, is at present in force and should certainly curb substitution, if even moderately well enforced.

Fifty years ago, 1887, while Idaho was still a territory, its legislative body passed a law (13), prohibiting the substitution of a different article for any article prescribed or ordered or otherwise deviating from the terms of the prescription or order, declaring such to be a misdemeanor, in case human life or health is endangered, or a felony if death ensues. These contingencies look serious but in fact provide loopholes for chronic substituters. The same law was enacted (14) in Arizona in 1901 and for Porto Rico in 1902 (15). The penalties in this law in a measure resemble those in the 1881 New York Law.

The State of Maine passed an excellent short law in 1899 (16) covering substitution in the filling of physicians' written prescriptions. It reads as follows: "Whoever, engaged in the business of an apothecary, knowingly uses any drugs or ingredients in preparing or compounding a written prescription of any physician different from those named in the prescription, shall upon conviction be fined not less than five nor more than one hundred dollars." This law commends itself for its brevity, simplicity, definiteness and fairness to all concerned. Such a law, if fairly enforced, is bound to minimize and possibly eradicate the malicious practice of substitution, in time.

In 1901 the legislature of Tennessee made it unlawful (17) to substitute any drug or medicine for the one mentioned in the physician's prescription, or aiding or abetting in committing the offense. The fine on conviction is not less than twenty-five dollars nor more than one hundred dollars for each and every conviction.

Under the 1901 drug adulteration law (18) of Illinois, any person who substitutes or causes to be substituted, without notification to the purchaser, one material for another, shall be liable to prosecution under this act and if convicted shall be liable for all of the expenses incurred by the Board of Pharmacy, and in addition, for the first offense, shall be liable to a fine of not less

than fifty dollars nor more than one hundred dollars. Fines for each subsequent offense are not less than seventy-five dollars nor more than one hundred and fifty dollars.

In 1907 the law was amended (19) to include substitution in the filling of prescriptions This law is still in effect. The idea of the dispenser notifying the purchaser in case of substitution in the filling of prescriptions is rather unique and one is prompted to inquire as to its practicability. The enforcement of this act was lodged (20) with the Department of Registration and Education in 1917.

The anti-substitution law of Maryland, passed (21) in 1902, forbids knowingly selling or delivering of any medicine or drug to any person, other than that called for or ordered by such person, or using any drug or medicine other than that called for in a physician's prescription. A violation is adjudged a misdemeanor and a conviction thereof is punishable by a fine of not less than one hundred dollars nor more than five hundred dollars, or correspondingly severe imprisonments, or both such fines and imprisonments and in addition any person so convicted forfeits "the right to practice Pharmacy under any certificate or registration issued under the laws of this State." This is one of the early, if not the earliest, drastic anti-substitution laws.

North Carolina enacted an anti-substitution law (22) in 1937, along the lines of the Maryland act. A violation is adjudged a misdemeanor and on conviction thereof is punishable as such. The law contains an interesting proviso. It reads: "This Act shall apply to registered drug stores and their employees only." What the purpose of this restriction is, few are able to make out.

A review of the above summary of the state anti-substitution laws calls to mind the unsatisfactory conditions that prevailed in the states in the matter of food and drug adulteration, prior to the enactment of the national law. It is believed that some action should be taken to bring about uniform state anti-substitution laws and methods for their enforcement. It is therefore suggested that the chairman of this section appoint a committee of three, to study the subject during the coming year and make a report at the next annual meeting of the association.

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(11) *Ibid.*, page 553 (1881).

(12) *Ibid.*, page 1500 (1907).

(13) Idaho, Rev. Stat., page 744 (1887).

(14) Arizona, Rev. Stat., page 1246 (1901).

(15) Porto Rico, Rev. Stat., and Codes (Penal Code), page 552 (1902).

(16) Maine Public Laws, page 107 (1899).

(17) Tennessee Acts, Chap. 27, page 41 (1901).

(18) Illinois Laws, page 238 (1901).

(19) *Ibid.*, 382 (1907).

(20) Illinois Civil Administration Code, 3, 7 (1917).

(21) Maryland Laws, page 148 (1902).

(22) North Carolina Public Laws, Chap. 59, page 103 (1937).