

AMENDING FEDERAL NARCOTIC LAWS TO APPLY TO A RECENTLY DISCOVERED SYNTHETIC DRUG (ISONI- PECAINE)

JUNE 21 (legislative day, MAY 9), 1944.—Ordered to be printed

Mr. GEORGE, from the Committee on Finance, submitted the following

REPORT

[To accompany H. R. 4881]

The Committee on Finance, to whom was referred the bill (H. R. 4881) to amend the Internal Revenue Code, the Narcotic Drugs Import and Export Act, as amended, and the Tariff Act of 1930, as amended, to classify a new synthetic drug, and for other purposes, having considered the same, report favorably thereon without amendment and recommend that the bill do pass.

The situation which this bill is designed to meet requires prompt legislative action to make existing Federal narcotic laws applicable to a recently discovered synthetic drug. The general purpose of the bill and an explanation of the bill by sections is set forth in the report of the Committee on Ways and Means of the House of Representatives (H. Rept. No. 1583, 78th Cong., 2d sess.), which is included herein and made a part of this report.

[H. Rept. No. 1583, 78th Cong., 2d sess.]

The Committee on Ways and Means, to whom was referred the bill (H. R. 4881) to amend the Internal Revenue Code, the Narcotic Drugs Import and Export Act, as amended, and the Tariff Act of 1930, as amended, to classify a new synthetic drug, and for other purposes, report favorably thereon with an amendment and recommend that the bill, as amended, do pass.

The amendment is as follows:

Page 5, lines 4 through 8, strike out the sentence "The word 'isonipecaïne' as used in this paragraph shall mean any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic

acid ethyl ester, or any salt thereof, by whatever trade name designated.", and substitute in lieu thereof the following:

The words "isonipecaine" and "marihuana" as used in this paragraph shall have the same meaning as defined in sections 3228 (e) and 3238 (b), respectively, of the Internal Revenue Code.

This bill is designed to meet the situation which requires prompt legislative action to make existing Federal narcotic laws applicable to a recently discovered synthetic drug. The committee has been advised that this synthetic drug has an effect similar to morphine upon the human organism, although it has no appreciable chemical similarity to morphine; and that scientific experimentation in this country has disclosed that this drug possesses addiction liability comparable to morphine.

The committee was advised that isonipecaine was first synthesized in Germany where it was called Eudolat. The name was later changed to Dolantin and it was first manufactured by Germany's I. G. Farbenindustrie under German patent No. 695,216. Demerol is the trade-mark name of the synthetic drug substitute for morphine manufactured in this country under United States patent No. 2,176,151 and distributed for sale throughout the United States by the owner of the patent, the Winthrop Chemical Co.

As "Demerol" has been trade-marked as a brand name, it should not be employed in legislation. It was necessary, therefore, to coin a name to fit this synthetic drug, which name would be descriptive of it. The term "isonipecaine" is deemed a suitable designation. Since this new synthetic drug belongs to the general class of alkaloids, of which morphine is a representative, the name should end in "ine", and as this drug is a derivative of a chemical known as isonipecotic acid, the first eight letters of this term should be used. The suffix is joined to it by the letter "a" for euphonic purposes. The term "isonipecaine" as defined in the bill would include the drug identified by the trade-mark Demerol and any derivative or salt thereof, by whatever trade name designated.

It has been reported that the Winthrop Chemical Co. is producing Demerol for distribution in the United States at a rate of 300 ounces daily, or approximately 240,000 ounces annually, while the production of morphine in this country is only 100,000 ounces annually.

Demerol is said to bear no chemical relationship to morphine or any other product obtained from opium, but it has definite morphinelike physiological characteristics and is recommended by its sponsors for use in the practice of medicine, in cases where morphine might be indicated, to accomplish the same purposes as morphine. The committee is informed that scientific experimentation has revealed that Demerol (identified as "isonipecaine" in the bill) possesses addiction liability comparable to morphine. There is attached as an appendix excerpts from the Journal of the American Medical Association and various clinical and pharmacological reports, which establish that Demerol possesses the liability of producing physical dependence similar to that caused by morphine and similar addiction liability. Therefore, it is believed that, unless subjected to the same enforcement control as morphine, the manufacture, distribution, and use of this new synthetic drug will soon be productive of serious abuses, with inevitable spread of drug addiction. This danger has already

been recognized and steps have been taken to safeguard the distribution and use of this synthetic drug in several other countries where it has been introduced as a medicine. Isonipecaïne, known under a variety of trade names, has been subjected to the same control as morphine in Canada, Argentina, Mexico, Brazil, Colombia, and even in Germany where the drug was discovered.

The bill would amend various sections of existing law to subject isonipecaïne to the same restrictions as morphine with respect to manufacture, distribution, importation, and exportation. The most important of these restrictions is that of limiting retail sales to those made only pursuant to a practitioner's prescription issued in good faith for medical purposes.

The legislation has been recommended to the Congress by the Treasury Department and has the approval of the Bureau of the Budget. Your committee believes that the proposed legislation is meritorious and recommends its prompt passage.

EXPLANATION OF BILL

SECTION 1

Section 2550 of the Internal Revenue Code provides for a tax of 1 cent per ounce on opium, coca leaves, any compound, salt, derivative or preparation thereof, produced in or imported into the United States, and sold or removed for consumption or sale. This tax is represented by narcotic commodity tax stamps, which are to be affixed to the bottle or other container. Section 1 of the proposed bill would make the new synthetic drug, described as "Isonipecaïne", and any compound, salt, derivative or preparation thereof, subject to this tax and the control incident thereto.

SECTION 2

Section 2553 of the Internal Revenue Code prohibits the purchasing, selling, dispensing, or distributing of certain drugs except in or from the original stamped package, and further provides that "the absence of appropriate tax-paid stamps for any of the aforesaid drugs shall be prima facie evidence of a violation" by the person in whose possession same may be found. Section 2 of the proposed bill would correct an error in phraseology which appears in the above quotation. The word "for" appears therein, and the word "from" was originally enacted by the Revenue Act of 1918 (40 Stat. 1037, 1130). The correction of this word is desired to assure the statutory presumption of guilt provided for in the first instance by the Congress, and as held to be valid by the Supreme Court of the United States in *Thomas J. Casey v. United States* (1928, 276 U. S. 413).

SECTIONS 3 AND 9

Paragraphs 5 and 6 of section 2557 (b) of the Internal Revenue Code, derived from sections 1 and 2 of the act of August 12, 1937 (50 Stat. 627), and sections 1 and 2 of that act also codified in the United States Code, title 21, sections 200 and 200a, provide additional punishment for second, third, and subsequent offenses for selling, importing,

or exporting, or conspiring to sell, import, or export, opium, coca leaves, cocaine, or any salt, derivative, or preparation thereof, in violation of the laws of the United States. Sections 3 and 9 of the proposed bill would add the synthetic drug called isonipecaine to the drugs enumerated above.

SECTION 4

Section 2558 of the Internal Revenue Code provides for the confiscation and disposal of opium, its salts, derivatives, and compounds, and coca leaves, salts, derivatives, and compounds thereof, seized by the Government from any person charged with any violation of the provisions of the Internal Revenue Code relating to narcotics and of the Narcotic Drugs Import and Export Act, as amended (U. S. C., title 21, secs. 171-185). Section 4 of the proposed bill would merely enlarge the scope of this section by adding the new synthetic drug identified as isonipecaine. This section of the proposed bill would also add the citations of three additional acts amending the Narcotic Drugs Import and Export Act to the list of acts enumerated therein that amend that act.

SECTIONS 5 AND 7

Section 3228 of the Internal Revenue Code defines several words as used in certain sections of the Internal Revenue Code pertaining to narcotics and coca leaves. Section 7 of the proposed bill would add to that section a definition of the word "Isonipecaine" as used in the sections of the Internal Revenue Code proposed to be amended. Section 5 of the proposed bill, which would amend section 2565 of the Internal Revenue Code, would add a necessary reference to section 3228. Isonipecaine would be defined to mean any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester, or any salt thereof, by whatever trade name designated. The common trade name in this country by which such substance is identified is Demerol, which is a trade-mark covering 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester.

SECTION 6

Sections 3220 and 3221 of the Internal Revenue Code require every person who imports, manufactures, produces, compounds, sells, deals in, dispenses, or gives away opium or coca leaves, or any compound, manufacture, salt, derivative, or preparation thereof, to register with the Collector of Internal Revenue and to pay an occupational tax. Section 6 of the proposed bill would require every such person who engages in such activities with isonipecaine, or any compound, manufacture, salt, derivative, or preparation thereof, to comply with these restrictions.

SECTION 8

Section 1 of the Narcotic Drugs Import and Export Act, as amended (U. S. C., title 21, sec. 171), defines various terms as used in that act. The term "narcotic drug" is defined to mean opium, coca leaves, cocaine, or any salt, derivative, or preparation of opium, coca leaves, or cocaine. Section 8 of the proposed bill would add isonipecaine to the enumeration in this term, and define the word "Isonipecaine" as used therein.

SECTION 10

Section 10 of the proposed bill would amend section 584 of the Tariff Act of 1930, as amended (U. S. C., title 19, sec. 1584), by enlarging the scope of the penalty imposed by that section against vessels carrying unmanifested heroin, morphine, or cocaine so as to include isonipecaine. Section 584, at present, provides a penalty of \$50 an ounce against the master or owner of a vessel upon which is found unmanifested heroin, morphine, or cocaine. In addition, section 10 of the proposed bill would enlarge the scope of the penalty imposed against vessels carrying unmanifested smoking opium prepared for smoking, to include marihuana. The committee amendment is a technical amendment incorporating in the Tariff Act of 1930 a definition of the term marihuana and isonipecaine by reference to specific sections of the Internal Revenue Code. A penalty of \$25 an ounce is imposed under existing law for unmanifested smoking opium. At the present time the only control over the importation of marihuana is an internal revenue tax. In view of the fact that marihuana grows abundantly in many foreign countries, and as its danger has been recognized in this country, it is urged that marihuana be included under the \$25 penalty clause.

CHANGES IN EXISTING LAW

In compliance with paragraph 2a of rule XIII of the Rules of the House of Representatives, changes in existing law made by the proposed legislation are shown as follows (existing law proposed to be omitted is enclosed in black brackets; new matter is in italics):

(Internal Revenue Code) SEC. 2550. TAX.

(a) RATE.—There shall be levied, assessed, collected, and paid upon opium, *isonipecaine*, coca leaves, any compound, salt, derivative, or preparation thereof, produced in or imported into the United States, and sold, or removed for consumption or sale, an internal revenue tax at the rate of 1 cent per ounce, and any fraction of an ounce in a package shall be taxed as an ounce. The tax imposed by this subsection shall be in addition to any import duty imposed on the aforesaid drugs.

(b) BY WHOM PAID.—The tax imposed by subsection (a) shall be paid by the importer manufacturer, producer, or compounder.

(c) HOW PAID.—

(1) STAMPS.—The tax imposed by subsection (a) shall be represented by appropriate stamps, to be provided by the Secretary.

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(Internal Revenue Code) SEC. 2553. PACKAGES.

(a) GENERAL REQUIREMENT.—It shall be unlawful for any person to purchase, sell, dispense, or distribute any of the drugs mentioned in section 2550 (a) except in the original stamped package or from the original stamped package; and the absence of appropriate tax-paid stamps [for] from any of the aforesaid drugs shall be prima facie evidence of a violation of this subsection by the person in whose possession same may be found; and the possession of any original stamped package containing any of the aforesaid drugs by any person who has not registered and paid special taxes as required by sections 3221 and 3220 shall be prima facie evidence of liability to such special tax.

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(Internal Revenue Code) SEC. 2557. PENALTIES.

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(b) VIOLATIONS IN GENERAL.—

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(5) A person who, after having been convicted of selling, importing, or exporting, or conspiring to sell, import, or export, opium, coca leaves, cocaine, *isonipecaine*, or any salt, derivative, or preparation of opium, coca leaves, [or] cocaine, or *isonipecaine*, again sells, imports, or exports, or conspires to sell, import, or export, any of the said narcotic drugs, in violation of the laws of the United States, shall, upon conviction of such second offense, be fined not more than \$5,000 or imprisoned in a Federal penitentiary for not more than ten years, or both, in the discretion of the court, whenever the fact of such previous conviction is established in the manner prescribed in paragraph 7 of this subsection.

(6) A person who, after having been two times convicted of selling, importing, or exporting, or conspiring to sell, import, or export, opium, coca leaves, cocaine, *isonipecaine*, or any salt, derivative, or preparation of opium, coca leaves, [or] cocaine, or *isonipecaine*, again sells, imports, or exports or conspires to sell, import, or export, any of the said narcotic drugs, in violation of the laws of the United States, shall, upon conviction of such third offense, or any offense subsequent thereto, be fined not more than \$10,000 or imprisoned in a Federal penitentiary for not more than twenty years, or both, in the discretion of the court, whenever the fact of such previous convictions is established in the manner prescribed in paragraph 7 of this subsection.

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(Internal Revenue Code) SEC. 2558. FORFEITURES.

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(b) SEIZED OPIUM—CONFISCATION AND DISPOSAL.—

(1) PROCEDURE.—All opium, [its salts, derivatives, and compounds, and coca leaves, salts, derivatives, and compounds thereof,] *coca leaves, isonipecaine, and all salts, derivatives, and preparations of opium, coca leaves, and isonipecaine*, seized by the United States Government from any person or persons charged with any violation of this chapter or part V of subchapter A of chapter 27, or the Act of February 9, 1909 (ch. 100, 35 Stat. 614), as amended by the Act of January 17, 1914 (ch. 9, 38 Stat. 275), the act of May 26, 1922, c. 202, 42 Stat. 596, the Act of June 7, 1924, c. 352, 43 Stat. 657, and the Act of June 14, 1930, c. 488, 46 Stat. 586 (U. S. C., title 21, §§ 171-184), shall upon conviction of the person or persons from whom seized be confiscated by and forfeited to the United States; and the Secretary is authorized to deliver for medical or scientific purposes to any department, bureau, or other agency of the United States Government, upon proper application therefor under such regulation as may be prescribed by the Secretary, any of the drugs so seized, confiscated, and forfeited to the United States. The provisions of this paragraph shall also apply to any of the aforesaid drugs seized or coming into the possession of the United States in the enforcement of this chapter, part V of subchapter A of chapter 27, or any of the above-mentioned acts where the owner or owners thereof are unknown. None of the aforesaid drugs coming into possession of the United States under the operation of said chapter, part, or acts, or the provisions of this paragraph, shall be destroyed without certification by a committee appointed by the Secretary that they are of no value for medical or scientific purposes.

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(Internal Revenue Code) SEC. 2565. DEFINITIONS.

For definitions of the following, see the subsections of section 3228 indicated below:

PERSON—

Subsection (a).

IMPORTER, MANUFACTURER, OR PRODUCER.—

Subsection (b).

WHOLESALE DEALER.—

Subsection (c).

RETAIL DEALER.—

Subsection (d).

ISONIPECAINE.—

Subsection (e).

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(Internal Revenue Code) SEC. 3220. TAX.

On or before July 1 of each year every person who imports, manufactures, produces, compounds, sells, deals in, dispenses, or gives away opium, [or] coca leaves, or *isonipecaine*, or any compound, manufacture, salt, derivative, or preparation

thereof, shall pay the special taxes hereinafter provided. Every person upon first engaging in any of such activities shall immediately pay the proportionate part of the tax for the period ending on the following June 30.

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(Internal Revenue Code) SEC. 3228. DEFINITIONS.

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(e) *ISONIPECAINE*.—The word “isonipecaïne” as used in this part and subchapter A of chapter 23 shall mean any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester, or any salt thereof, by whatever trade name designated.

Subsection (a) of section 1 of the Narcotic Drugs Import and Export Act, as amended (U. S. C., title 21, sec. 171):

When used in this Act—

(a) The term “narcotic drug” means opium, coca leaves, cocaine, *isonipecaïne*, or any salt, derivative, or preparation of opium, coca leaves, [or] cocaine, or *isonipecaïne*; and the word “isonipecaïne” as used herein shall mean any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester, or any salt thereof, by whatever trade name designated.

* * * * *

The act of August 12, 1937 (50 Stat. 627, U. S. C., title 21, sec. 200):

A person who, after having been convicted of selling, importing, or exporting, or conspiring to sell, import, or export, opium, coca leaves, cocaine, *isonipecaïne*, or any salt, derivative, or preparation of opium, coca leaves, [or] cocaine, or *isonipecaïne*, again sells, imports, or exports, or conspires to sell, import, or export, any of the said narcotic drugs, in violation of the laws of the United States, shall, upon conviction of such second offense, be fined not more than \$5,000 or imprisoned in a Federal penitentiary for not more than ten years, or both, in the discretion of the court, whenever the fact of such previous conviction is established in the manner prescribed in section 3 of this Act. The word “isonipecaïne” as used in this section shall mean any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester, or any salt thereof, by whatever trade name designated.

SEC. 2. A person who, after having been two times convicted of selling, importing, or exporting, or conspiring to sell, import, or export, opium, coca leaves, cocaine, *isonipecaïne*, or any salt, derivative, or preparation of opium, coca leaves, [or] cocaine, or *isonipecaïne*, again sells, imports, or exports or conspires to sell, import, or export, any of the said narcotic drugs, in violation of the laws of the United States, shall, upon conviction of such third offense, or any offense subsequent thereto, be fined not more than \$10,000 or imprisoned in a Federal penitentiary for not more than twenty years, or both, in the discretion of the court, whenever the fact of such previous convictions is established in the manner prescribed in section 3 of this Act. The word “isonipecaïne” as used in this section shall mean any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester, or any salt thereof, by whatever trade name designated.

The second paragraph of section 584 of the Tariff Act of 1930 as amended (U. S. C., title 19, sec. 1584):

If any of such merchandise so found consists of heroin, morphine, [or] cocaine, or *isonipecaïne*, the master of such vessel or person in charge of such vehicle or the owner of such vessel or vehicle shall be liable to a penalty of \$50 for each ounce thereof so found. If any of such merchandise so found consists of smoking opium [or], opium prepared for smoking, or *marihuana*, the master of such vessel or person in charge of such vehicle or the owner of such vessel or vehicle shall be liable to a penalty of \$25 for each ounce thereof so found. If any of such merchandise so found consists of crude opium, the master of such vessel or person in charge of such vehicle or the owner of such vessel or vehicle shall be liable to a penalty of \$10 for each ounce thereof so found. Such penalties shall, notwithstanding the proviso in section 594 of this Act (relating to the immunity of vessels or vehicles used as common carriers), constitute a lien upon such vessel which may be enforced by a libel in rem; except that the master or owner of a vessel used by any person as a common carrier in the transaction of business as such common carrier shall not be liable to such penalties and the vessel shall not be held subject to the lien, if it appears to the satisfaction of the court that neither the

master nor any of the officers (including licensed and unlicensed officers and petty officers) nor the owner of the vessel knew, and could not, by the exercise of the highest degree of care and diligence, have known, that such narcotic drugs were on board. Clearance of any such vessel may be withheld until such penalties are paid or until a bond, satisfactory to the collector, is given for the payment thereof. The provisions of this paragraph shall not prevent the forfeiture of any such vessel or vehicle under any other provision of law. *The words "isonipecaïne" and "marihuana" as used in this paragraph shall have the same meaning as defined in sections 3228 (e) and 3238 (b), respectively, of the Internal Revenue Code.*

APPENDIX

(1) Demerol—A new synthetic analgesic—A Review of its Present Status and Comparison with Morphine. By Robert C. Batterman, M. D., New York, and C. K. Himmelsbach, M. D., surgeon, United States Public Health Service, Lexington, Ky. (Published in Journal of the American Medical Association, vol. 122, No. 4, May 22, 1943.)

"With the exception of the production of cough and diarrhea, Demerol has been found to be a satisfactory therapeutic substitute for morphine. It appears to possess the following clinical advantages over morphine:

1. Its spasmolytic action makes it ideal for the relief of conditions due to smooth muscle spasm, in which morphine is pharmacologically contraindicated.
2. Its rapid dissipation tends to offset undesirable cumulative effects such as respiratory depression and urinary retention.
3. Prolonged use of Demerol may lead to the development of habituation, but it appears to possess a lesser liability than morphine for the development of physical dependence.

"In order to avoid the dangers of habituation, physical dependence and undue cerebral irritability, amounts greater than 150 mg. every 3 hours should not be given. We wish to reemphasize the point that, if this amount will not meet the clinical need, increasing the dose and shortening the interval not only may not have any additional therapeutic value but is apt to result in serious consequences."

(2) Demerol—Clinical Observations. By Drs. Hans Hecht, Paul H. Noth, and F. F. Yonkman of Detroit. (Published in Journal of the American Medical Association, vol. 121, No. 16, April 17, 1943.)

"Demerol, a synthetic substance, is apparently capable of replacing morphine and its derivatives to a certain extent, thus helping to relieve a possible future shortage of opiates. Demerol is not toxic even when given in large doses over a prolonged period. Occasional side effects are observed, and long continued use may be followed by undesirable symptoms on withdrawal."

(3) Cortical Effects of Demerol. By Dr. H. L. Andrews, United States Public Health Service Hospital, Lexington, Ky. (Published in the Journal of Pharmacology and Experimental Therapeutics, vol. 76, No. 1, September 1942.)

"Demerol is a drug which has a profound effect on the central nervous system when used in quantities sufficient to satisfy the desires of addicts. These effects are of such a nature that serious harm might come to those who could obtain the drug in quantities sufficient to meet such requirements. If the drug were freely available abuse might occur, for all patients considered most of the effects pleasant and desirable, and stated that the discomforts following withdrawal were sufficient to discourage voluntary discontinuance."

(4) Studies of the Addiction Liability of Demerol. By Dr. C. K. Himmelsbach, United States Public Health Service Hospital, Lexington, Ky. (Published in the Journal of Pharmacology and Experimental Therapeutics, vol. 75, No. 1, May 1942.)

"When substituted for morphine, Demerol partially satisfied the physical dependence established to morphine. On withdrawal, after 10 days of substitution, a definite but mild abstinence syndrome occurred.

"Physical dependence on Demerol resulted from its regular administration to post-addicts over a period of 10 weeks. The abstinence syndrome which occurred following its withdrawal was milder than the morphine abstinence syndrome but otherwise quite typical. The duration of the physical dependence action of Demerol was considerably shorter than that of morphine.

"Conclusion: Demerol possesses addiction liability."

(5) Further Studies of the Addiction Liability of Demerol. By C. K. Himmelsbach, United States Public Health Service Hospital, Lexington, Ky. (Published in the Journal of Pharmacology and Experimental Therapeutics, vol. 79, No. 1, September 1943).

"Since it appears probable that Demerol will soon enjoy wide therapeutic use, it is appropriate to reiterate that so far as addiction liability is concerned the difference between Demerol and morphine is largely in degree, not kind. It might be most unfortunate if the impression became popular that Demerol is non-habit-forming. Similar erroneous impressions surrounded the introduction of heroin and dilaudid and resulted in unjustified optimism and addiction in patients who should have been spared both. An analogous situation developed in certain Provinces of Canada before the sale of codeine was restricted. Hence, physicians should be enjoined to employ Demerol with the same degree of caution that should be given to prescribing morphine. With such caution the beneficial effects of the drug would not be minimized appreciably and the occurrence of addiction to Demerol in the bona fide practice of medicine should be rare."

CONCLUSIONS

1. Demerol possesses the liability of producing physical dependence similar to that caused by morphine.

2. In clinical doses the addiction liability of Demerol is less than that of morphine.

3. As an addiction preventive measure, caution and restrictions similar to those involved in the clinical use of morphine should be applied to Demerol.

(6) Is Dolantin a Narcotic? by P. O. Wolff, M. D., Ph. D., Buenos Aires, Argentina:

"The analogy of action in the pharmacologic researches was so evident that Schaumann stated, in a hypothesis, that it existed because of the fact that the skeleton of dolantin is found in the structure of morphine, as it is found out when the structure of both substances is carefully compared * * *.

"Druckrey of the Institute of Pharmacology of the Faculty of Medicine of Berlin (Med. Klinik, vol. 37, No. 35, p. 885, 1941) stated that shortly after dolantin was introduced on the market cases were reported of patients who used large amounts of the drug. An exaggerated use of the drug was also reported from Switzerland.

"Reports on certain particular cases confirmed the analgesic and spasmodic effects of the drug. Several authors compare the analgesic effect of the drug with that of morphine, and suggest the possible narcotic effects of the drug * * *.

"Kucher (Klin. Wschr., vol. 19, p. 688, 1940) reported two cases of habituation to dolantin, which were observed in patients in a well known sanatorium of Berlin. One of the patients was a woman who for 10 years was an addict to morphine. Later on she became an addict to dolantin when she suffered the fracture of an arm. She used even 10 ampules a day. The clinical picture of her disease was very complicated and she did not exhibit precise symptoms of abstinence. The other patient was an addict to eucodal. Since she knows dolantin she has been able to renunciate the administration of opium derivatives. She uses even 24 ampules of dolantin by the intravenous route. She felt marked euphoria. When she suddenly interrupted the use of the drug she exhibited symptoms of abstinence. The second case shows clearly the development of dolantin addiction which originated in eucodal addiction and associated with dolantin euphoria. * * *

"Von Brucke (Wien. Klin. Wschr. 1940, No. 42, p. 854) reports two cases of dolantin addiction in which the patients used the drug as a substitute to morphine and dionin, respectively.

"Drs. Nerio Rojas and Jose Belbey, regular professors of legal medicine at the Faculties of Medicine of Buenos Aires and La Plata, respectively, in lectures recently delivered before the Sociedad de Medicina Legal y Toxicologia reported three cases of dolantin addiction as a substitute of morphine addiction (Arch. de Medicina Legal, vol. 11, No. 3, pp. 212-217, 1941). In one of the cases the patient increased the doses of dolantin during habituation and exhibited the well-known picture of necessity. The second and third patients rapidly became habituated to the use of large doses of dolantin. In the second patient diminution of the doses failed. The third patient used even 22 ampules a day.

"According to the lecturers, habituation to dolantin is rapidly produced in morphine addicts. The patients exhibit physical and psychical phenomena of real need of the drug and have dolantin injections with frequency because of the fact that the effect of dolantin is less prolonged than that of morphine.

"Dr. Luis E. Silva reported, in the same reunion, two more cases of his clinetele. One of the patients was an addict to morphine, which was substituted by dolantin. He even used 15 daily ampules. The other patient was an asthmatic woman who had previously resorted to any narcotic (primary dolantin addiction). She used 5 or 6 daily ampules. If she is not allowed to use the drug she exhibits headaches and some other symptoms of necessity of the drug.

"Dr. Diogenes Garda (Dia Medico, Buenos Aires, June 10, 1941, p. 1053) made observations on two patients with chronic narcotic addiction. The patients used dolantin injections for 2 months. They exhibit symptoms of abstinence with excitement and anxiety which were sedated by the administration of an opium preparation * * *.

"The relative brevity of action of dolantin is due to its rapid disintegration in the body. It results in a frequent need and in increasing the doses when it is used for a long time. These facts explain habituation to dolantin * * *.

"Dr. H. Fischer, professor of pharmacology of the Faculty of Medicine of Zurich carried on some researches by order of the Federal Department of Public Hygiene. He concluded that the action of dolantin is similar to that of morphine, namely as an opium preparation * * *.

"The claims of the firm which prepares dolantin, namely, (1) that large doses of the drug do not cause unpleasant effects and (2) that it is the first synthetic compound which is free from narcotic substances, are unjustified.

"In well verified cases, habituation and symptoms of abstinence of the drug have been verified. The aspect of habituation is not altered even by the cases reported in which it did not occur. * * * The few cases in which habituation is not formed are of no importance, when they are compared with the large number in which habituation occurred."

(7) Dolantin, a New Spasmolytic and Analgesic (Chemical and Pharmacological Considerations), by O. Eisleb and O. Schaumann. (Published in Deutsche Medizinische Wochenschrift 65, 967 (1939).

"The chemical and pharmacological properties of 1-methyl-4-piperidine-4-carboxylic acid-ethyl ester-hydrochloride (Dolantin) are briefly discussed. In this compound was noted the combination spasmolytic properties of atropine and papaverine with an analgesic efficacy of morphine-like character."

(8) Two Cases of Dolantin Addiction, by Ilse Kucher (Klinische Wochenschrift, 19, 688 (1940)).

"Various authors point to the fact that an habituation, or the development of an addiction on increasing the dose, was never observed. This view is not correct. We ourselves have observed two cases in which the abuse of Dolantin resulted in addiction. We have heard of similar observations made by others."

(9) Dolantin and Habituation, by Dr. Nerio Rojas, titular professor of legal medicine, Faculty of Medicine, Buenos Aires, and Dr. Jose Belbey, titular professor of legal medicine, University of La Plata. Presented at Fourth Ordinary Session of the Society of Legal Medicine and Toxicology, July 23, 1941. (From Archivo de Medicina Legal, 11, 212 (1941).)

"In the face of these facts we believe ourselves authorized to reach the following conclusions:

" 'Dolantin is an excellent analgesic and antispasmodic.

" 'In morphine addiction its use as a therapeutic substitute is dangerous as the patient falls into a veritable dolantin addiction in a much shorter time and with higher and more frequent doses.

" 'It is necessary to be prudent in all cases in which the continuity of the pathological cause compels frequent repetition of the drug as it is necessary continually to increase the dose and the number of injections which may bring about habituation.

" 'The sale of dolantin must not be free, and it must be made only by medical prescription.' "

