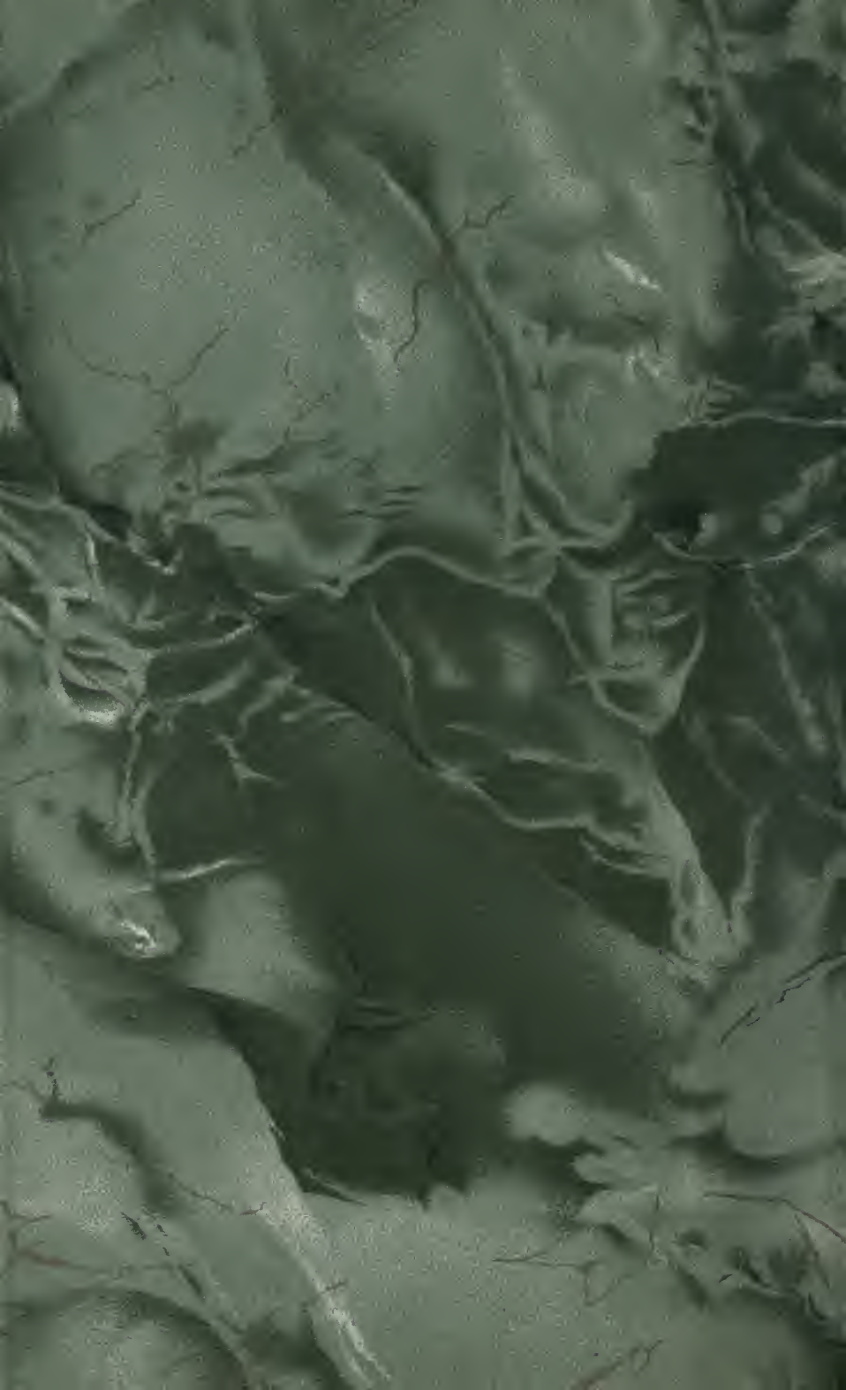

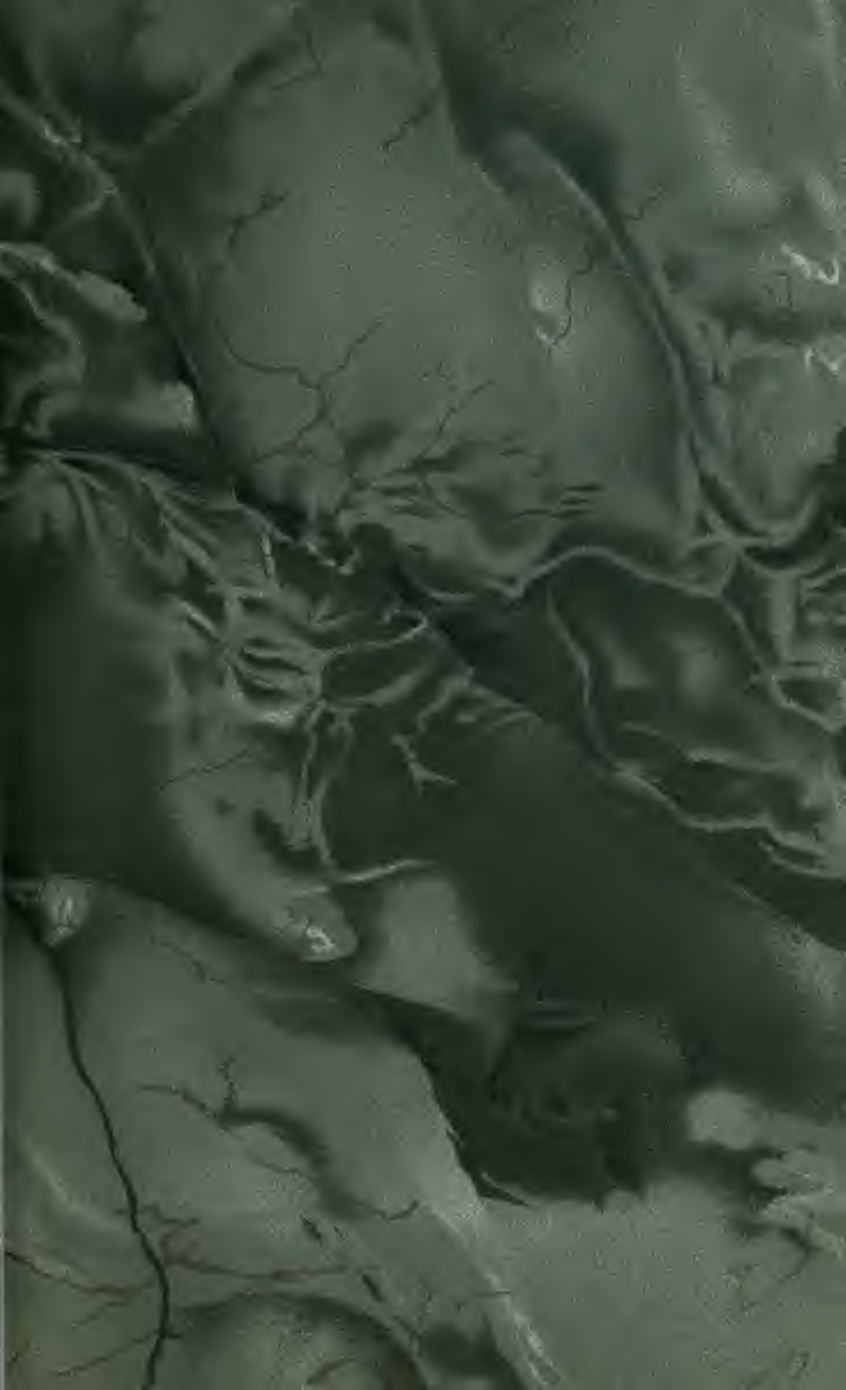

ANNUAL REPRINT OF THE REPORTS

OF THE

COUNCIL ON PHARMACY AND CHEMISTRY

OF THE

AMERICAN MEDICAL ASSOCIATION

FOR 1918

WITH THE

COMMENTS THAT HAVE APPEARED
IN THE JOURNAL

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PREFACE

This volume—the Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association — contains the reports of the Council that have been adopted and authorized for publication during 1918. It includes reports of the Council previously published in THE JOURNAL, along with such editorial comments as have accompanied them. In addition, the volume contains reports of the Council which, because of their lesser importance, were not published in THE JOURNAL, and which as a matter of record are included here. That the Council's official reports may be made available to physicians, chemists, pharmacologists and others interested in medicine, the Council authorized publication of this volume.

John Harper Long — An Appreciation

The following has been unanimously adopted by the members of the Council on Pharmacy and Chemistry.

W. A. PUCKNER, Secretary.

WHEREAS, Death has called from a life of useful service to science and to humanity Dr. John Harper Long, professor of chemistry in the Northwestern University Medical School and a member of the Council on Pharmacy and Chemistry of the American Medical Association; and

WHEREAS, He devoted his life to the development of the chemical phases of medicine, both as a teacher and as a pioneer investigator in his chosen field, and served for many years as a most faithful and conscientious member of the Council on Pharmacy and Chemistry; be it therefore

Resolved, That we, members of the Council on Pharmacy and Chemistry of the American Medical Association, extend our deepest sympathy to his bereaved wife and family; and be it further

Resolved, That these resolutions be recorded in the minutes of the Council, and that copies be sent to THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, and to his family.

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REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY

MEDEOL SUPPOSITORIES

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., March 9, 1918, p. 719

The following report on Medeol Suppositories has been adopted by the Council, and its publication authorized.

W. A. Puckner, Secretary.

"Medeol Suppositories" (Medeol Company, Inc., New York) appear to be an imitation of "Anusol Suppositories" which, in 1907, were found to be inadmissible to New and Nonofficial Remedies. A comparison of the composition and of the claims made for the two preparations will be of interest in the present consideration of Medeol Suppositories:

Anusol Suppositories (1909)		Medeol Suppositories (1917)	
Anusoli	7.5	Medeol	0.25
Zinc oxid	6.0	Zinc Oxid	0.5
Balsam Peru	1.5	Acid. Tannic	0.15
Ol. theobrom.	19.0	Bals. Peru	0.16
Ungt. cerat.	2.5	Cocoa Butter and wax *q. s.*	
for 12 suppositories		for 1 suppository.	

"Anusol" was formerly said to be bismuth iodoresorcinsulphonate. The A. M. A. Chemical Laboratory published a report in 1909 showing that the suppositories contained only 1 per cent. of the iodin declared in the "formula," and were greatly deficient in bismuth and sulphur. After the publication of the report the American agents for the product disclaimed that "Anusol" was a definite chemical compound. Today Anusol Suppositories are said to contain unstated amounts of the indefinite "bismuth oxyiodid and resorcinsulphonate."

"Medeol" is said to be "resorcinated iodo bismuth," but no information is vouchsafed as to the character or composition of the ingredient. The therapeutic claims made for the two preparations are similar, as the following, taken from circulars, show:

ANUSOL SUPPOSITORIES

An innocuous, non-irritant remedy for anal, rectal and vaginal inflammatory affections, especially for HEMORRHOIDS!

The local medicinal treatment of hemorrhoidal and other inflammatory ano-rectal conditions has always been unsatisfactory. The usual media cannot be applied in effective concentration without producing intense inflammatory reactions; they are either ineffective or intolerable. . . .

Anusol suppositories are absolutely free from narcotic, caustic or other injurious ingredients and may unhesitatingly be used by both sexes, at any age and under all conditions.

MEDEOL SUPPOSITORIES

An innocuous, Non-irritant, Efficient Antiphlogistic for use in inflammatory diseases of the rectum, anus and vagina especially in HEMORRHOIDS.

Hitherto most of the local remedies used in these conditions have either been too irritating to be employed in sufficient concentration to be efficient or they have lacked efficiency per se. . . .

Medeol suppositories do not contain any narcotic or any caustic or other constituent having violent action; their blandness permits of their use in either sex and at all ages.

The claims made for these preparations—as for instance "that surgical treatment . . . should rarely be undertaken until Medeol Suppositories have been given a thorough trial" —are misleading in that they create the inference that the limitations in the palliative treatment of piles have been overcome. It is altogether untrue that these mixtures can be expected to "relieve the most obstinate cases," as stated in a Medeol circular. This, from an Anusol circular, is equally mileading:

"If dietetic and other requirements are complied with, even the most obstinate chronic cases will frequently readily yield to treatment with Anusol Suppositories."

The Council declared Medeol Suppositories inadmissible to New and Nonofficial Remedies because their composition is secret (Rules 1 and 2); because unwarranted therapeutic claims are made for these (Rule 6); because the name is objectionable (Rule 8), and because the combination is unscientific (Rule 10).

In those cases of hemorrhoids in which palliative measures may be expected to enable the patient to avoid surgical interference and afford relief from attacks, the object should be to secure cleanliness, to avoid irritation, whether it be by friction or irritating fecal matter, to reduce inflammation by astringents and, when necessary, to relieve pain by analgesics. If an antiseptic dusting powder is desired, boracic acid in impalpable powder with talc may be employed; if an astringent, finely powdered oxid of zinc may be added; if a local analgesic is necessary, a little extract of belladonna may be incorporated with petrolatum or other ointment base. The main reliance, in any event, should be to effect normal bowel

movements by regulating the diet rather than by the use of purgatives; the use of warm water to insure cleanliness; the avoidance of irritation, especially that caused by friction and secretions; a mild astringent to reduce inflammation.

[EDITORIAL NOTE.—During the past year advertisements of Anusol Suppositories appeared in the following medical journals:

Medical Record
Boston Medical & Surgical Journal
Woman's Medical Journal
Interstate Medical Journal
American Journal of Surgery
Medical Review of Reviews
Medical Council
New York Medical Journal
American Medicine
International Journal of Surgery
Urologic and Cutaneous Review
Critic and Guide
Journal-Lancet

Advertisements of Medeol Suppositories appeared with a good deal of regularity during the past year in the following:

International Journal of Surgery
American Medicine
Medical Record
New York Medical Journal
Medical Times]

GUAIODINE

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., April 6, 1918, p. 1026

The following report on Guaiodine, marketed by the Intravenous Products Company, Denver, has been adopted by the Council and its publication authorized.

W. A. PUCKNER, Secretary.

A referee of the Committee on Pharmacology, in submitting to the Council a report from the A. M. A. Chemical Laboratory on Guaiodine, advises that the Laboratory's examination shows that instead of containing free "colloidal" iodin as claimed, the preparation is essentially an iodated fatty oil, containing only combined iodin. Equally misleading, in view of the Laboratory's findings, are the implied claims that the antiseptic action of Guaiodine corresponds to that of free iodin.

Guaiodine is advertised mainly for the treatment of gonorrhea. While it may be true that the guaiacol contained in Guaiodine has some beneficial effect, especially when preceded by potassium permanganate irrigation as advised, the advertised claim that "Guaiodine acts as a specific for gonorrhea in a majority of cases" is utterly false.

The "'case records" offered to establish the therapeutic value of Guaiodine are in themselves sufficient to condemn the "evidence." The following are fair samples:

"The second boy came a day or so later with a slight discharge with the characteristic burning and itching, and with symptoms of a beginning gonorrhea, and judging from the source of the infection, it was believed to be so. Two injections of Guaiodine were given when the discharge ceased."

"I have several cases that were completely cured in a very short time. I note this, that the first dose causes a cessation of the discharge and the second seems to increase the flow, but the color is changed. I give three doses, and then use a mild wash, and in ten days they are well. I am very pleased with this preparation and very truly believe that it is the best there is to date for the positive cure of gonorrhea."

REPORT OF THE CHEMICAL LABORATORY

Guaiodine is manufactured by the Intravenous Products Company, Denver, Colorado. The "literature" which accompanies the product describes Guaiodine as:

". . . an electro-chemically prepared iodin, suspended in oil, containing iodin, the same strength as the U. S. P. tincture of iodin, or 7 per cent., together with a therapeutic dose of guaiacol."

The Intravenous Products Company claims that Guaiodine is made by an "electro-chemical process of preparing colloidal iodine," discovered by one E. B. Page, and that by this process the tendency of iodin to produce iodism has been "overcome." It is said to be "pre-eminently an antiseptic and germicide." Guaiodine is a dark brown, oily liquid with a specific gravity of 0.9845 at 15.6 C. and an odor suggestive of guaiacol. Its solubilities were those of a fat. Free iodin was absent in the recently purchased specimen (traces were present in an older one). Steam distillation indicated that the product consisted of volatile and nonvolatile constituents. The volatile matter was concluded to consist, in the main, of guaiacol or some guaiacol-like body, and the nonvolatile matter to be an iodized fatty oil. Quantitative determinations indicated that Guaiodine contained about 7.25 per cent. of iodin in combination, and that it is composed approximately of 3 per cent. volatile matter and 97 per cent. nonvolatile matter. Hence Guaiodine appears to be an iodized fatty oil to which a small amount of guaiacol or some guaiacol-like substance has been added.

THE COUNCIL'S ACTION

On the recommendation of the referee, the Council voted that Guaiodine be declared inadmissible to New and Nonofficial Remedies because of false statements as to composition and action.

[EDITORIAL NOTE.—Advertisements of Guaiodine have appeared, during the past year, in the following:

New York Medical Journal
Medical Review of Reviews
Military Surgeon
American Medicine
Urologic and Cutaneous Review
Therapeutic Gazette
American Journal of Surgery
Medical Times
International Journal of Surgery
American Journal of Clinical Medicine]

PYOCYANEUS BACILLUS VACCINE OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., May 18, 1918, p. 1486

The Council has authorized publication of the following report. W. A. PUCKNER, Secretary.

Pyocyaneus bacillus vaccine, made from *Bacillus pyocyaneus,* was admitted to New and Nonofficial Remedies in 1910. At that time this vaccine was considered to give promise of having therapeutic value.

Now three of the firms whose preparations of this vaccine are described in New and Nonofficial Remedies advise the Council that they have ceased to manufacture the vaccine because of lack of demand. The fourth firm stated that in the printing of a new list of its biologic products, pyocyaneus vaccine would not be included, and that the preparation would be supplied on demand only.

The referee of the Committee on Serums and Vaccines in charge of pyocyaneus bacillus vaccine held that the discontinuance of the preparation by interested firms, for the reason that there was no demand for it, evidences that it had been proved without value. He reported that a search of recent literature failed to reveal any evidence of its usefulness.

On the recommendation of the referee, the Council directed that the several preparations of the vaccine be omitted from New and Nonofficial Remedies.

SEVERAL "MIXED" VACCINES NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., June 23, 1918, p. 1967

The "mixed" vaccines which are discussed in the reports that follow were considered by the Council during the past year because inquiries had been received in regard to them.

In publishing these reports it is desirable that the attitude of the Council toward "mixed" vaccines again be stated. In view of the rapid development of bacterial therapy, the possibility for harm that attends the use of bacterial vaccines and the skepticism among experienced clinicians as to the value of vaccines representing a combination of organisms, the Council has felt that it should scrutinize the claims for such agents with exceptional care and that there should be admitted to New and Nonofficial Remedies only

those vaccine mixtures for which there is acceptable evidence to indicate that the use of the particular mixtures is rational.

In considering the subject the Council has borne in mind the fact that in many institutions in which cases are studied and the results of therapeutic measures carefully observed and controlled, vaccines of any sort are practically never used—certainly here the stock mixed vaccine has no recognition. Experienced clinicians have generally come to the conclusion that mixed vaccines have no specific action and that any effect they may produce is due to a non-specific protein reaction.

As set forth in the reports, in no case was the evidence submitted by the proprietors sufficient to establish the claims made for the preparations. Hence none was accepted for New and Nonofficial Remedies.

The preparations that form the basis for the accompanying reports are only a few of the many that are being made and sold by some biological houses. Doubtless many of those not dealt with in this report are equally irrational and sold under claims equally—or probably even more—unwarranted than those with which the present report deals.

W. A. PUCKNER, Secretary.

Mixed Vaccines-Abbott

In response to inquiry the Council undertook a consideration of the following "mixed" vaccines sold by the Abbott Laboratories:

M. Catarrhalis-Combined-Bacterin, said to contain killed Micrococcus catarrhalis, Bacillus Friedländer, Pneumococci, Streptococci, Staphylococcus aureus and Staphylococcus albus.

B. Coli-Combined-Bacterin, said to contain killed Streptococcus viridans, Streptococcus hemolyticus and Bacillus coli.

Pertussis-Combined-Bacterin, said to contain killed Bacillus pertussis, Pneumococci, Streptococci, Staphylococcus albus, Staphylococcus aureus and Micrococcus catarrhalis.

Streptococcus-Rheumaticus-Combined-Bacterin, said to contain killed "Streptococci (Rheumaticus, Viridans, etc.)" and Pneumococci.

Streptococcus-Viridan-Combined-Bacterin, said to contain killed Streptococcus viridans, Streptococcus hemolyticus, Pneumococcus and Staphylococcus albus.

The Abbott Laboratories were asked to assist in the investigation of these products and to submit evidence to establish their eligibility for admission to New and Nonofficial Remedies. The manufacturer was informed that the Council

accepts "mixed" vaccines or bacterins, provided the usefulness of these products is established by acceptable clinical evidence, and references to the literature bearing on the value of the preparations were requested.

The Abbott Laboratories submitted specimens of the products, the advertising matter therefor and a considerable list of references to current literature; all of which was transmitted to the Committee on Serums and Vaccines for consideration. In due time a referee of the committee submitted the following report:

THE COMMITTEE'S REPORT

The referee has studied the literature covered by the references submitted. In general the articles are favorable to the use of vaccines, though many of these papers do not consider "mixed" vaccines; indeed, a number of the articles do not discuss treatment at all, but are devoted entirely to the consideration of etiology of the disease. Many of the papers are by those who are obviously overenthusiastic on the subject of the use of biologic preparations. One paper—not included in the references submitted by the Abbott Laboratories—records an alarming reaction following a dose of mixed vaccine; no claim is made that improvement followed:

The following comments on the submitted references are offered:

M. Catarrhalis - Combined - Bacterin. — Only four of the nine references given deal with the therapeutic use of the vaccine. The reported results in general were favorable, but sometimes in the discussion evoked by certain of the papers, views the reverse of those expressed by the author were brought forward. The enthusiasm of one writer is shown in his statement that following the use of vaccine in cases of carbuncle complicating diabetes the sugar in the urine disappeared or was reduced. One observer, who reports excellent results in nasal and pharyngeal catarrh, speaks of certain vaccines as "bulk goods," while another considers "——'s No. 7" as the proper thing. It is evident that the reports are not based on careful, scientific data, or such unscientific definition of the product employed would not be used.

B. Coli-Combined-Bacterin.—In the references cited in support of this preparation the following general statements are noted: One enthusiastic writer says, "It must be recognized that we have no satisfactory explanation of the action of vaccines, and their use at present is empirical." One author dwelt on the superiority of autogenous vaccines but admits that occasionally stock vaccines are indicated. One vaccine therapist in concluding an article states, "It is simply impossible to practice modern urology without our modern biologic products." Yet it is a well-known fact that many

successful and capable genito-urinary surgeons avoid the use of vaccines, mixed or simple.

Pertussis-Combined-Bacterin.—These reports are uniformly favorable, but are not controlled and their value is not to be compared with a recent report from the New York City Department of Health which indicates that the vaccine is practically valueless. It is noted, further, that one of the articles cited which dealt rather fully with the treatment of pertussis did not mention vaccines.

Streptococcus-Rheumaticus-Combined-Bacterin. — The references cited in support of the preparations by the manufacturer give no support whatever for the use of mixed stock vaccines. The first reference deals with the relation of Streptococcus viridans to arthritis deformans and endocarditis and reports the following cases:

Case 1.—Vaccine case—improvement after eight months.
Case 2.—Slight improvement following use of vaccine.
Case 3.—Slight improvement following use of vaccine.
Case 4.—Marked improvement.
Case 5.—Prompt improvement.
Case 6.—Vaccine not mentioned.
Case 7.—Vaccine followed by slight improvement.

In each of the cases other methods of treatment were used. The paper shows the etiologic relation of Streptococcus viridans rather than the value of vaccines. There is no indication that stock vaccines were used, though the paper is not clear on this point. The second paper deals with the application of vaccine therapy in the treatment of arthritis. This paper is by a man who is avowedly an enthusiast on vaccine therapy. The indications are that he generally used a mixed autogenous vaccine, but the reports of cases are not always clear. This writer apparently makes no serious attempt at the classification of the joint conditions he treats. The third reference is a purely experimental study and has no bearing on the use of vaccines in treatment. The fourth article was admitted by the manufacturer to be "negative as regards evidence." The fifth reference specifically states that "the vaccine must be autogenous." The sixth reference deals with the experimental production of appendicitis by the use of diplococci, and has not the most remote bearing on the use of vaccines in the treatment of rheumatism.

Streptococcus - Viridans - Combined - Bacterin.—The article which bears evidence of more care than the others admits that we are not in position to state the value of vaccines in pyorrhea but the author believes they may have value supplementary to local treatment.

It is not surprising that a large number of favorable reports can be accumulated when we appreciate how promptly men report what they consider to be their successes and how commonly they leave their failures unrecorded. Bearing in mind the fact that these stock mixed vaccines, though before the profession for many years, have not been used,

or continued in use, in hospitals where work is rigidly controlled and that they are used practically not at all in the large government hospital service, a candid critic must hold that there is no substantial evidence in favor of the therapeutic use of a mixed vaccine, certainly not for stock "goods" and that probably there is but a limited field for the employment of autogenous vaccines.

The referee calls attention to a shift in the advertising matter on vaccines—the tendency to recommend vaccines to be used in conjunction with drugs. A heading in the Abbott booklet reads, "The Biologics Do Not Replace Drugs"; and the paragraph speaks of serums and bacterins as "new tools, supplemental to those we already have, but not replacing them." . . . "We need them both."

The referee recommends that the several mixed vaccines discussed in this report be not accepted on the grounds that satisfactory evidence of their value is wanting.

Having been endorsed by the Committee on Serums and Vaccines the Council adopted the report and declared M. Catarrhalis-Combined-Bacterin, B. Coli-Combined-Bacterin, Pertussis - Combined - Bacterin, Streptococcus - Rheumaticus-Combined - Bacterin and Streptococcus-Viridans-Combined-Bacterin ineligible for admission to New and Nonofficial Remedies.

Catarrhal Vaccine Combined-Lilly and Influenza Mixed Vaccine-Lily

Because of inquiry received, the Council requested Eli Lilly and Company to aid in determining the acceptability of the following products for New and Nonofficial Remedies: "Catarrhal Vaccine Combined," said to contain killed cultures of the Bacillus of Friedländer, Micrococcus catarrhalis, Staphylococcus aureus and albus, Pneumococcus and Streptococcus; "Influenza Mixed Vaccine," said to contain killed cultures of Staphylococcus albus and aureus, Streptococcus, Pneumococcus, Micrococcus catarrhalis and Bacillus influenzae.

Lilly and Company sent the circulars, etc., used in advertising these products. A circular for "Catarrhal Vaccine Combined" contained the following claim:

"Catarrhal Vaccine has been especially useful in many respiratory infections, including bronchitis, pharyngitis, rhinitis, chronic catarrh and in the mixed infections of pulmonary tuberculosis."

A circular for "Influenza Mixed Vaccine" contained the following:

"The vaccine is useful in the treatment of influenza and ordinary colds, and in any infection in which the Bacillus influenzae is the causative agent."

An advertising pamphlet contained the following:

"Catarrh, Acute and Chronic; Colds, Influenza.—The micro-organisms capable of producing catarrhal conditions of the nose and pharynx and most commonly isolated are B. Friedländer, M. catarrhalis, staphylococcus, pneumococcus (in infections beginning in the larynx), *B. influenza* and streptococcus. These organisms are found normally in the respiratory passages and acquire virulence only when resistance has been lowered through overwork, exposure to cold, etc.

"The results following the use of Catarrhal Vaccine Combined (in the non-epidemic forms) and influenza Mixed Vaccine (in the epidemic types) have been very satisfactory, due to the great vascularity of the tissues. Acute attacks are aborted altogether or shortened in duration and the danger of complications greatly minimized."

No evidence was submitted which warrants the preceding claims nor is the Council aware of any reliable testimony to indicate that the administration of the mixture here discussed is warranted or desirable. On the recommendation of the Committee on Serums and Vaccines the Council voted that "Catarrhal Vaccine Combined-Lilly" and "Influenza Mixed Vaccine-Lilly" be not included in New and Nonofficial Remedies because satisfactory evidence of their value is wanting.

Influenza Serobacterin Mixed-Mulford

Because of inquiry received, the Council took up the consideration of "Influenza Serobacterin Mixed-Mulford," and requested the Mulford Company to present evidence to establish the admissibility of the preparation to New and Nonofficial Remedies. The Mulford Company sent specimens of the serobacterin in question, an advertising circular and a letter by the director of its Biologic Laboratories.

According to the label on the package, the preparation is made from the following organisms: Bacillus influenzae, Staphylococcus aureus, Staphylococcus albus, Streptococcus, Pneumococcus and Micrococcus catarrhalis (group). This mixture is recommended by the manufacturer:

"For the prophylaxis and Treatment of Common Colds, Mixed Infections of the Respiratory Mucous Membranes, Acute and Chronic Catarrhal Conditions of the Nose, Throat and Respiratory Passages."

No evidence is submitted for this recommendation except that in "colds and bronchitis and the other common infections of the upper respiratory passages . . . five or six bacteria are very commonly present—two or more of them are nearly always present . . ." and the letter by the director of the Mulford Biologic Laboratories expressing the belief that in his own case the use of the mixed vaccine has aborted or prevented colds.

As regards the use of this complex biologic preparation:

First, the cause of common colds is, at the present time, quite unknown. One of the most striking things is that at the beginning of a cold the organisms to be cultivated from the nasal mucous membrane are very few in number and there is no uniformity in the type of organism found. If some one of the well-known organisms (Streptococcus, Staphylococcus, Pneumococcus, Micrococcus Catarrhalis, Influenza Bacillus, etc.) were responsible, we should expect to find one of them preponderating and in overwhelming numbers. This is far from the case. After the duration of the cold for a day or two with the increased production of mucus and apparently with the infection of a mucous membrane whose powers of resistance have been greatly lowered, bacteria of all kinds are to be found in immense numbers. There is considerable reason for believing that an ultramicroscopic organism is responsible for this condition (See Foster, *Journal of Infectious Diseases* **21**:451 [Nov.] 1917).

Second, there is no acceptable clinical evidence that vaccination with the influenza bacillus, the Streptococcus, the Pneumococcus or the Micrococcus Catarrhalis will influence the course of an infection due to one or the other of these organisms. It has been repeatedly found that a staphylococcus vaccine is of a certain degree of value when the infection with the staphylococcus is localized, but it is well known that general systemic infections with the staphylococcus are not at all benefited.

Third, the letter submitted as evidence by the Mulford Company is not convincing. The Council is not prepared to accept evidence of this sort unless it is in volume large enough to justify a definite conclusion.

Holding that there is no evidence for the value of this mixture, the Council declared "Influenza Serobacterin Mixed-Mulford" inadmissible to New and Nonofficial Remedies because its use is illogical.

Sherman's Mixed Vaccine No. 40

Because of inquiry received the Council decided to consider this preparation and requested the manufacturer, G. H. Sherman, Detroit, Mich., to submit evidence in support of the claims made for it.

This vaccine is said to be made from killed cultures of Streptococcus, Pneumococcus, Micrococcus catarrhalis, Staphylococcus aureus, and Staphylococcus albus. In the printed matter sent out by G. H. Sherman this vaccine is recommended for hay-fever, in which it is stated that some of

the symptoms are due to bacterial invasion of the respiratory mucosa; for tonsillitis, both as a remedy and as a prophylactic against rheumatic and other sequelae; for "throat infections"; for rhinitis with the claims that acute coryza can be aborted within twenty-four hours; for pneumonia in which it is advised for all stages; for laryngitis, for bronchitis, and for asthma.

No acceptable evidence was submitted as to the value of the product in the treatment of any of the foregoing conditions. In view of what is known about non-specific reactions, it seems likely that any influence which this vaccine may have on the diverse conditions enumerated by the manufacturer, is due to this, rather than to the combination of organisms used in its preparation.

On the recommendation of the Committee on Serums and Vaccines, the Council declared "Sherman's Mixed Vaccine No. 40" ineligible to New and Nonofficial Remedies because the therapeutic claims made for it are unwarranted (Rule 6) and because the combination, in view of its complexity, is irrational and detrimental to sound therapy (Rule 10).

CHLORIN-SODA AMPOULES

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., July 6, 1918, p. 39

The report of the Association's Chemical Laboratory which appears below was submitted to the Council by a referee. The Council endorsed the report and authorized its publication. The Council also voted to accept Chlorin-soda Ampoules for New and Nonofficial Remedies.

W. A. Puckner, Secretary.

THE EXAMINATION OF CHLORIN-SODA AMPOULES

Report of the A. M. A. Chemical Laboratory

H. D. Dakin, in conjunction with A. Carrel and M. Daufresne, has introduced the so-called "Neutral Solution of Chlorinated Soda," or "Dakin's Solution," different standards and modes of preparation having been described. It is essentially a solution containing from 0.45 to 0.50 per cent. sodium hypochlorite, in a hypertonic solution of sodium chlorid and sodium carbonate and sodium bicarbonate. To prepare the solution, as they describe, requires that the available chlorin content of the chlorinated lime used be known, and that the available chlorin content of the finished solution be checked by titration. To obviate this, various preparations

have been placed on the market, claiming to yield, when made according to direction, a solution having the correct strength of hypochlorite and to be "neutral" to phenolphthalein.

Johnson and Johnson offer "Chlorin-soda Ampoules" composed of (A), a sealed glass tube stated to contain 4.8 gm. liquid chlorin having a purity of "approximately over 99 per cent.," and (B), a sealed glass tube stated to contain 21.3 gm. monohydrated sodium carbonate U. S. P. The contents of "B" are placed in a 2.5 liter bottle, and dissolved in 1 liter of water. Tube "A," containing the liquid chlorin, is suspended from the inserted rubber stopper. The large bottle is then vigorously shaken, breaking the chlorin ampule.

Some of the claims made for the product are:

"The Johnson and Johnson method in a few seconds gives the Carrel-Dakin antiseptic solution of standard strength of between 0.45 per cent. and 0.50 per cent. of sodium hypochlorite, free from caustic alkali.

"All settling, decantation and filtering to eliminate lime sludge is avoided; the solution is exact and definite; all necessity for, and the trouble of an analytical test is obviated.

"The Carrel-Dakin solution resulting from this method is perfectly clear and ready for immediate use.

"The method is thus at once adaptable to hospital and field use, as well as to ordinary office practice."

"It is not necessary to make analysis of the solution made up from liquid chlorin by the Johnson and Johnson method, but for those who wish to check up the strength we state that it must contain between 0.45 per cent. and 0.50 per cent. sodium hypochlorite and that this is determined by titrating 10 c.c., in the presence of an excess of potassium iodide and acetic acid, with tenth-normal sodium hyposulphite and that the amount of this hyposulphite solution necessary ranges between 12.0 c.c. and 13.4 c.c.

"The test for caustic alkalinity, as prescribed, consists in throwing some powdered phenolphthalein upon the surface of some of the solution in a beaker and twirling the beaker to mix it. No red color should be produced."

One original package containing three ampules each of chlorin and of "Soda Salts" was sent to the Council by Johnson and Johnson, and another original package was purchased on the open market.

The liquid chlorin was brown, and was contained in colorless hard glass ampules about 7 inches long and ⅜ inch in diameter. The following quantitative determinations were made:

Chlorin Ampule.—The chlorin was allowed to escape from one tube by opening the pointed end, with due precautions, by heating. The loss in weight of the ampule was 4.600 gm. chlorin. A very small yellow residue remained in the tube.

Sodium Carbonate Ampules.—The weight of the contents of four "soda" ampules was 21.7, 21.5, 21.6 and 21.5 gm., respectively; average, 21.5 gm.

By titration (*a*) 2.6336 gm. required 41.60 c.c. normal hydrochloric acid solution, equivalent to 97.98 per cent. monohydrated sodium carbonate; (*b*) 2.2295 gm. required 35.90 c.c. normal hydrochloric acid solution, equivalent to 99.70 per cent. monohydrated sodium carbonate; average, 98.9 per cent.

Sodium Hypochlorite Solution.—The directions given by Johnson and Johnson were followed in preparing the hypochlorite solutions. The titrations were also carried out according to the method described by Johnson and Johnson (essentially the U. S. P. assay method for Solution of Chlorinated Soda).

(A) The chlorin tube broke near the middle, developing pressure, and some chlorin escaped: (*a*) 10 c.c. of the solution required 9.88 c.c. of tenth-normal sodium thiosulphate solution, equivalent to 0.37 per cent. sodium hypochlorite; (*b*) 10 c.c. of the solution required 9.88 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.37 per cent. sodium hypochlorite.

(B) In preparing this sample, the chlorin tube also broke above the level of the water. As the stopper of the bottle was wired down no chlorin could escape at once. Yet when the stopper was taken out, after the bottle had been shaken for about one minute, the strong smell denoted that some uncombined chlorin had escaped: (*a*) 10 c.c. required 10.35 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.38 per cent. sodium hypochlorite; (*b*) 10 c.c. required 10.16 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.38 per cent. sodium hypochlorite.

(C) In preparing this sample, the chlorin tube broke near the lower end. After shaking the contents two minutes, no free chlorin escaped, when the stopper was released: (*a*) 10 c.c. of the solution required 13.3 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.49 per cent. sodium hypochlorite; (*b*) 10 c.c. required 13.3 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.49 per cent. sodium hypochlorite.

(D) The procedure was the same as C and no chlorin escaped: (*a*) 10 c.c. required 12.8 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.47 per cent. sodium hypochlorite; (*b*) 10 c.c. required 12.8 c.c. tenth-normal sodium thiosulphate solution, equivalent to 0.47 per cent. sodium hypochlorite.

(E) The solution was prepared as above, and after shaking from one and one-half to two minutes, the stopper was released when chlorin escaped: (*a*) 10 c.c. required 12.8 c.c. of tenth-normal sodium thiosulphate solution, equivalent to 0.47 per cent. sodium hypochlorite; (*b*) 10 c.c. required 12.8 c.c. of tenth-normal sodium thiosulphate solution, equivalent to 0.47 per cent. sodium hypochlorite.

(F) This tube could not be broken when vigorously shaken inside of the large bottle. It was therefore removed, cleaned and dried, and the chlorin content determined as described above.

Stability of Solution after Forty-Eight Hours.—Solutions D and E were allowed to remain near a window on dark days for forty-eight hours. In solution D the strength of sodium hypochlorite was 0.46 per cent. In solution E there was no perceptible decrease.

Phenolphthalein Test.—All of the solutions gave no color with powdered phenolphthalein, as described by Dakin, although they did color an alcoholic phenolphthalein solution momentarily before it was destroyed.

DISCUSSION

If loss of chlorin is guarded against, Johnson and Johnson Chlorin-soda Ampoules will give a solution of the strength described by them. To insure this, the stopper should be wired down or otherwise secured firmly and the bottle shaken for at least two minutes after the chlorin ampule has been broken. As the chlorin is under considerable pressure, the ampules when broken, especially if the sealed end is short, are often greatly shattered so that due precaution should be taken to filter off the glass particles. The chlorin tubes would break easier, more surely and with less shattering of glass and less pressure, if the sealed end was either more uniformly drawn out to a longer and somewhat smaller point, or so modified that the breaking would occur at the narrow tip. (With regard to this, Johnson and Johnson write that precautions have been taken to draw out the point of the chlorin tube longer and finer, so that no trouble, on

this account, will occur in the future.) As Johnson and Johnson state that the chlorin contained in the ampules has a purity of over 99 per cent., it would be a valuable contribution if they would publish purity tests for the chlorin.

OPHTHALMOL-LINDEMANN

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., July 6, 1918, p. 59

Ophthalmol-Lindemann was taken up for consideration by the Council because of inquiries received. The following report, declaring Ophthalmol inadmissible to New and Nonofficial Remedies, was adopted by the Council and its publication authorized. W. A. PUCKNER, Secretary.

Ophthalmol-Lindemann (Innis, Speiden and Co., New York) is advertised as a treatment for eye diseases by "hyperemia." The circular advertising the product is written somewhat in the style of "patent medicine" advertisements. It contains testimonials of dubious value. The principle underlying the use of Ophthalmol is that employed to a considerable extent by ophthalmologists, through the use of ethylmorphine ("dionin"), etc., viz., the production of conjunctival irritation in inflammatory eye diseases. Ophthalmol is, therefore, merely a special agent for the production of such ophthalmic irritation.

The advertising circular contains no evidence that Ophthalmol is in any respect superior to the established agents for producing conjunctival hyperemia. On the other hand, there are obvious objections to the use in the eye of a substance of unknown and apparently indefinite composition and uncertain activity. Ophthalmol is said to be an oily solution of "glandular extract of the fish Cobitis Fossilis." *Cobitis fossilis* is a small fish said to be common in Germany. According to Kochs, who analyzed Ophthalmol (*Arb. a. d. Pharm. Inst. d. Univ. Berl.*, **4**:140, 1907), this fish is popularly believed to predict weather, but medical virtues are not ascribed to it. This "fishy" extract is indefinite, to say the least.

The activity of the preparation is described by the manufacturer thus: "It seems probable that the typical action of Ophthalmol is due to certain organic acids which may have formed during manufacture through the decomposition of protein bodies contained in the crude material." The profession is not told whether this important decomposition is, or, in fact, can be controlled so as to produce a material of uniform activity.

Kochs concluded from his analysis that Ophthalmol had the properties of rancid olive oil containing about 6 to 7 per cent. mineral oil. The oil contained no nitrogen, left no ash on ignition and though traces of iodin were claimed to be present, no iodin could be found.

It is recommended that Ophthalmol be rejected first, because the use in the eye of an irritant of secret composition and uncertain activity is unscientific and against the interest of public health; second, because Ophthalmol is of secret composition (the composition claimed being practically meaningless), and, third, because no evidence has been submitted to substantiate its claimed superiority over established methods of treatment. The Council declared Ophthalmol inadmissible to New and Nonofficial Remedies.

SILVOL INELIGIBLE FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., July 13, 1918, p. 140

The following report on Silvol (Parke, Davis & Company) was adopted by the Council and its publication authorized.

W. A. Puckner, Secretary.

The Council took up the consideration of Silvol (Parke, Davis & Company) because of inquiries received. The following report was submitted by the referee in charge of silver preparations:

Silvol (Parke, Davis & Company) is a silver-protein preparation of the Argyrol type. Like Argyrol, it is said to contain about 20 per cent. of silver. The referee finds that, like Argyrol, it is nonirritant to the nasal mucosa in a 10 per cent. solution; does not precipitate with chlorid; dissolves in water readily; a 25 per cent. solution has a high specific gravity (Silvol, 1.137 at 20 C.; Argyrol, 1.147 at 20 C.), and is not very viscid (viscosity, 1.25). A 1:1,000 solution of Silvol is clear and about 50 per cent. deeper in color than a solution of Argyrol of the same strength.

Silvol differs from Argyrol mainly in that its solutions yield a fine precipitate with egg albumin (under suitable conditions), while Argyrol is nonprecipitant; and in that Silvol solutions are not so effectively decolorized by Lloyd's reagent.

The manufacturers did not reply to an inquiry with regard to the basis for the claims made for Silvol (see Appendix). The referee was therefore obliged to deduce these claims from the firm's advertising matter. About the same claims are made for the local use of Silvol as are generally made

for Argyrol. These may be accepted without detailed evidence in view of the similarity of the two preparations.

Its usefulness, as suggested in the advertising, when given by mouth "in the treatment of acute or chronic gastritis, gastric ulcer, or gastro-enteritis," or the efficacy of very dilute solutions (0.2 per cent.) against dysentery, etc., is doubtful and requires substantiation by evidence. The claims that Silvol is astringent, though nonirritant and noncoagulant, that it is a "powerful germicide" or even that it is a "powerful antiseptic," and that it may be used with advantage wherever "a silver salt is indicated," need substantiation. There is no proof of the assertions that Silvol is "the most efficacious of silver salts"; "the most efficient antiseptic," and "the most remarkable organic silver compound. . . ."

As the manufacturers have not presented any evidence for their highly improbable claims, and as they have not signified any intention of making their claims agree with substantiated facts, it is recommended that Silvol be declared inadmissible to New and Nonofficial Remedies.

The Council adopted the report of its referee and authorized its publication.

APPENDIX

The following letter from the Secretary of the Council was sent to Parke, Davis & Company, March 20, 1917. No reply to it has been received:

The referee of the Council who is conducting an investigation of silver preparations asked me to inquire if you are willing to submit your evidence for the following claims which are made in your circulars for Silvol:

1. How it is possible for the solution to be astringent, and at the same time nonirritant and noncoagulant?

2. That intestinal irrigation with a Silvol solution containing 10 to 15 grains to the pint is sufficiently bactericidal to "be used in the abortive treatment of such infectious processes as dysentery, cholera infantum, and colitis."

3. What evidence have you as to the degree of antiseptic and germicidal power of Silvol solutions?

4. What evidence have you as to the degree of antiseptic and germicidal power of 5 per cent. Silvol Ointment?

A reply to the above questions and any other information in regard to Silvol will receive careful consideration.

KATHARMON

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Aug. 10, 1918, p. 487

Following inquiries, the Council took up "Katharmon" for consideration and authorized publication of the following report.

W. A. PUCKNER, Secretary.

The Katharmon Chemical Company of St. Louis in advertising its Katharmon appeals especially to a profession whose members, should they live up to their ethical code, could not prescribe it.[1] In 1893 (when the publication of "a formula" for proprietary preparations was thought to satisfy the requirements of scientific medicine) an advertisement in THE JOURNAL of the American Medical Association gave the following "formula" for Katharmon:

"Hydrastis Canadensis, Phytolacca Decandra, Acid Salicylous C. P. (from Oil of Wintergreen), Acid Boric C. P., Mentha Arvensis, Thymus Vulgaris, Dist. Ext. Hamamelis Virg. Conc."

In 1907 an advertisement in the Kansas City *Medical Index-Lancet* declared that:

"Katharmon represents in chemical combination the active principles of Hydrastis Canadensis, Gaultheria Procumbens, Hamamelis Virginica, Phytolacca Decandra, Mentha Arvensis, Thymus Vulgaris, with two grains C. P. Boric Acid to each fluid drachm."

Now the advertisements which appear in some medical journals state:

"KATHARMON represents in combination Hydrastis Canadensis, Thymus Vulgaris Mentha Arvensis, Phytolacca Decandra, 10½ grains Acid Borosalicylic, 24 grains Sodium Pyroborate to each fluid ounce of Pure Distilled Extract of Witch Hazel."

A comparison of these so-called formulas shows that they have not only varied from time to time, but that in no instance was a quantitative statement with regard to all the asserted ingredients given.

The Chemical Laboratory of the A. M. A. reports: Katharmon has an alkaline reaction and therefore cannot contain boric acid, salicylic acid or "borosalicylic acid" (the latter is unknown to medical literature except as loosely applied to a simple mixture of boric and salicylic acids). The solution gives tests for sodium, borate, and salicylate and therefore probably contains sodium borate and sodium salicylate. Examined by the methods used for the determination of hydrastin in goldenseal preparations, a residue giving only a faint test for alkaloid was obtained; if present at all, hydrastis canadensis (goldenseal) is there only in very small amounts.

A circular wrapped with the trade package of Katharmon contained the following, palpably unwarranted, claims:

"INTERNALLY it is very useful in acute indigestion, Gastric Catarrh, Diarrhoea and Cholera Infantum."

". . . it has demonstrated its remarkable curative effects, not only in preventing unhealthy conditions of fresh wounds, but also in

1. ". . . it is equally unethical to prescribe or dispense secret medicines or other secret remedial agents, . . ." Sec. 6, Art. I, Chapter II, *Principles of Medical Ethics*.

correcting the decaying of putrefactive processes peculiar to the body under certain circumstances. It has, further, a remarkable efficacy in surface inflammations, whether produced by accident or disease, and is an indispensable remedy in the affections of the mucous membranes of the nose, mouth, stomach, bowels, vagina, uterus, urethra, bladder and rectum."

Katharmon is in conflict with Rules 1 and 4 of the Council on Pharmacy and Chemistry because of its indefinite and secret composition and the method of advertising it indirectly to the public; it is in conflict with Rules 10, 6 and 8, in that it is an irrational shotgun mixture sold under unwarranted therapeutic claims and under a name nondescriptive of its composition.

IODINIZED EMULSION (SCOTT) AND CREOSOTONIC (SCOTT)

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Aug. 24, 1918, p. 680

"Iodinized Emulsion (Scott)" and "Creosotonic (Scott)" are proprietary preparations of the Dawson Pharmacal Company, Dawson Springs, Ky. The latter preparation used to be known as "Iodinized Emulsion (Scott) with Hypophosphites, Guaiacol and Creosote." In 1907 these preparations were considered by the Council and found inadmissible to New and Nonofficial Remedies. Examination of the preparations having been again requested, the Council considered them anew because the composition and claims had been changed somewhat and because at the previous consideration no report was published.

The reports which appear below were sent to the Dawson Pharmacal Company for comment before publication. In reply the company offered to revise its claims for the preparations. The Council replied that the report sent explained that both preparations are irrational mixtures, and hence a revision of the claims would not make them eligible for New and Nonofficial Remedies. It advised that publication of the report would be withheld sixty days and that it would be revised if new information or evidence was submitted permitting such revision. After expiration of the stipulated postponement, the Dawson Pharmacal Company wrote that no new advertising matter had been prepared but that the old circulars were not being sent out.

As these irrational preparations were still sold and advertised to the medical profession and presumably used by some physicians, the Council directed publication of its report with this explanation.

W. A. Puckner, Secretary.

Iodinized Emulsion (Scott)

The label for Iodinized Emulsion (Scott) declares:

"Each fluidram contains: Alcohol, m. 4¾; Rectified Ol. of Turpentine, m. 3½; Iodin, gr. ⅛; Phenol, gr. ½; Glycerine and Elixir Lactated Pepsin with Aromatic Oils in the form of a perfect emulsion."

A circular, which gives what is asserted to be the composition of Iodinized Emulsion, declares that, among other ingredients, each fluidram contains "one and three quarters m. Tincture of Iodine." Both the statement on the label that the preparation contains "iodin" and the one in the circular that tincture of iodin is present in the product are incorrect, for the A. M. A. Chemical Laboratory reports that no free iodin could be detected in the preparation, and that it responded to tests for iodid instead.

An advertising circular for Iodinized Emulsion (Scott) makes unwarranted claims for the therapeutic properties of the constituents. For example:

". . . the great usefulness of Turpentine in diseases, especially of the Intestinal Infection, such as the Metcorism and Tympanites of Typhoid."

And this absurdity:

". . . where Turpentine, Carbolic Acid or Iodine or even Pepsin is indicated, that it will give satisfaction in each and every case."

Iodinized Emulsion (Scott) is not a "pharmaceutical triumph"; it is an irrational mixture—a reminder of a decadent polypharmacy—sold under misleading and unwarranted claims. It is inadmissible to New and Nonofficial Remedies for conflict with Rules 1, 6, 8 and 10.

Creosotonic (Scott)

Creosotonic (Scott), advertised as a "reconstructive tonic" for the tuberculous, according to the label, contains in each fluidram:

"Alcohol, m. 2½; Creosote and Guaiacol sulphonates of each, gr. 1; Compound Hypophosphites, gr. 1 (including Quinine Hypophosphites, gr. 1/36 and Strychnine Hypophosphites, gr. 1/256), with Iodinized Emulsion (Scott) m. 30."

As in the case of Iodinized Emulsion (Scott), the advertising makes exaggerated therapeutic claims for the individual constituents of the preparation and for the heterogeneous mixture of guaiacol and creosote sulphonates, hypophosphites, quinin, strychnin, turpentine, phenol, iodin, "lactated pepsin," etc. Thus, while it is well established that in guaiacol sulphonate and creosote sulphonate the phenolic constituent is bound so firmly that, when administered, but very little is split off in the organism, yet the advertising claims

"that the system can be saturated in a shorter time and with smaller doses of creosote and guaiacol sulphonates than with any other form of these drugs" and that (on the false premise that the guaiacol and creosote from these drugs will permeate the tissues of the lungs) "they help to clear up the local infection and thus aid in returning to normal the diseased mucous membrane."

In the advertising pamphlet, following a discussion of the effect of climate and food in the treatment of the tuberculous, we read:

"While admitting the great importance of the foregoing points, we are firmly of the opinion that proper medication is a great aid in the treatment of pulmonary tuberculosis, and, with this in view, we offer to the profession Creosotonic (Scott) believing that in it we have a superior preparation for this purpose."

This is unwarranted. Of course suitable medication to meet special conditions is proper in the treatment of tuberculosis, but the routine administration of a complex and irrational mixture such as Creosotonic (Scott) is bound to cause inattention to the prime requisites for the proper treatment of the tuberculous—hygienic surroundings and good food.

Creosotonic (Scott) is an irrational mixture, sold under misleading and unwarranted claims. It is inadmissible to New and Nonofficial Remedies for conflict with Rules 1, 6, 8 and 10.

CAMPETRODIN AND CAMPETRODIN NO. 2

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Sept. 21, 1918, p. 993

The following report on Campetrodin and Campetrodin No. 2 has been adopted by the Council and its publication authorized. W. A. PUCKNER, Secretary.

The following report of the A. M. A. Chemical Laboratory on "Campetrodin" and "Campetrodin No. 2," sold by the A. H. Robins Company, Richmond, Va., was submitted to the Council by a referee of the Committee on Pharmacology:

Campetrodin and Campetrodin No. 2, Double Strength, are called "ethical medicinal specialties" by the A. H. Robins Company, Richmond, Va., which sells them. An advertisement in the *Maryland Medical Journal* (December, 1917) contains the following claim for composition:

"CAMPETRODIN (Made in Two Strengths of Iodine). This preparation is an Oleaginous Solution of Iodine in Camphor."

A booklet describing the "specialties" of the Robins Company contains the following in reference to Campetrodin: "Composition: Camphor, Iodine Element, Oleaginous Solvent." From this it appears that the preparations are claimed to contain elementary (free) iodin in an "oleaginous solvent." Since free iodin, as is well known, readily combines with fats, it was decided to determine the form in which the iodin was present in these preparations. The examination demonstrated that both preparations contained but a trace of free iodin. On steam distillation there was obtained from both preparations a distillate amounting to about 35 per cent. by volume which had an odor strongly suggestive of turpentine, while the residue contained the iodin and had the characteristics of an iodized fatty oil.

Quantitative determinations indicated that Campetrodin contained approximately 0.03 per cent. of free iodin and 1.3 per cent. of iodin in combination with the fatty oil. Campetrodin No. 2, Double Strength, contained approximately 0.03 per cent. free iodin and 2 per cent. of iodin in combination with the fatty oil.

Thus, contrary to the published statements, Campetrodin is *not* a preparation of free (elementary) iodin, and Campetrodin No. 2, Double Strength, does *not* contain twice as much iodin as Campetrodin.

The report of the Chemical Laboratory shows that the statements made in regard to the composition of Campetrodin and Campetrodin No. 2 are incomplete in some respects and false in others. In view of the Laboratory's findings it appears superfluous to inquire into the therapeutic claims made for the preparations: It is evident, however, that a solution containing practically no free iodin is not, as claimed by the Robins Company, "adapted for use wherever . . . iodin is indicated externally. . . ."

It is recommended that Campetrodin and Campetrodin No. 2 be declared inadmissible to New and Nonofficial Remedies because of false statements as to chemical composition and therapeutic action, constituting conflicts with Rules 1 and 6.

The Council adopted the recommendation of the referee and authorized publication of this report.

CARMINZYM

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Sept. 28, 1918, p. 1081

The Council has authorized publication of the following which explains why Carminzym was not accepted for New and Nonofficial Remedies. W. A. PUCKNER, Secretary.

Carminzym is a tablet sold by Fairchild Bros. and Foster, New York. Each tablet contains,-according to claims made, approximately 32 mg. of an extract of pancreas, 50 mg. sodium bicarbonate, 172 mg. prepared chalk, 1.5 mg. powdered ipecac and "aromatics *q. s.*" Without consideraing other possible conflicts with its rules, the Council held the preparation inadmissable to New and Nonofficial Remedies for conflict with Rule 10 which holds that unscientific or useless articles are not acceptable products.

The Council holds that complex mixtures of remedial agents are, from every point of view, inimical to therapeutic progress and therefore to the public welfare. Such mixtures are especially objectionable because it is impossible accurately to determine the effects which follow the simultaneous administration of a number of drugs having dissimilar actions; because the practice of prescribing such mixtures tends to discourage careful consideration of the special needs of individual patients without which there can be no rational drug therapy. On the contrary, with the use of such mixtures therapeutic treatment becomes haphazard and mere guesswork.

The Council, appreciating that long established customs cannot be changed at once, has applied Rule 10 concerning the recognition of mixtures with the greatest leniency compatible with consistency. When there has been a reasonable doubt concerning the value of a mixture it has frequently directed that Rule 10 should not apply pending further clinical trial of such mixture. In no instance has subsequent experience shown that a strict interpretation of the rule would have worked hardship or injustice. The Council feels that there is no longer warrant for the admission of complex mixtures to New and Nonofficial Remedies or for the retention of any that have been admitted unless definite evidence of the therapeutic value of such combinations is available. In accordance with this decision several mixtures now described in New and Nonofficial Remedies will be omitted at the expiration of the three year period for which articles are accepted.

Reverting to the Carminzym tablet: When it is desired to obtain the effects of pancreatic extract by oral administration it must be administered with a view of preventing its destruction by the gastric fluid. With this end in view an antacid should be administered to decrease the acidity of the gastric juice. The amount of alkali may be supplied in the form of any of the official preparations, but the amount must be adjusted to the individual patient for the reason that no two

successive patients are likely to have the same degree of gastric acidity.

Ipecac has a well defined though limited field of usefulness. When it is used, it should be given with a due regard to the amount needed by the patient and the frequency of the repetition of the dose. There is no reason to suppose that any two successive patients will require ipecac and extract of pancreas in a fixed proportion and with equal frequency. As a matter of fact, the amount of ipecac in Carminzym is so small that no definite therapeutic action can be assigned to it and its use in this combination is purely empirical.

In a word, the employment of mixtures of pancreatic extract, alkalis, ipecac and carminatives in fixed proportion leads to slipshod treatment and irrational therapeutics. Carminzym is an irrational mixture the use of which is detrimental to therapy.

The preceding report was sent to Fairchild Bros. and Foster for comment in accordance with the Council's usual procedure. The following reply was received:

The long established custom of the use of mixtures of remedial agents rests upon considerations well known and generally accepted. This is equally true of combinations of drugs of similar and dissimilar properties. The drugs of these combinations, especially those of marked therapeutic action, are well known and used by themselves when indicated.

In fact, dissimilarity of action is a cause of combination, an essential of synergism.

Drugs classed as similar are by no means alike in action; laxatives, tonics, carminatives, diuretics are combined with distinct advantage, economy of dose, enhanced effect, potency not obtainable with the single drug.

Your sweeping arbitrary conclusions that complex mixtures of remedial agents are from every point of view inimical to therapeutic progress is not, it seems to us, sustained by fact and experience. There is therapeutic progress in the considerate use and observation of combinations as well as in the use of a single drug. Indeed, in the production of a synthetic chemical substance as a therapeutic agent, the combination of potent and dissimilar elements is worked out to mitigate and correct an objectionable side effect, and promote desirable action.

As for ourselves, at the very outset in our line of work we quite voluntarily declared our principles and our intentions as opposed to incompatible and therefore unstable or inert combinations of the enzymes; and against the "unnecessary multiplication of preparations" —see Fairchild's Hand-book of the Digestive Ferments.

Is not this after all the crux of the whole matter—does a combination contain the ingredients stated, does it possess the demonstrable properties which are to be attributed to it in consequence of this composition; and if for a certain purpose, is it well designed therefor?

Carminzym presents certain agents of well known properties, not in the least of incompatible or antagonistic action, but indeed especially suitable for the particular purpose designed; its efficacy not to be

measured and judged by theory or opinion as to the efficiency of a certain dosage of a particular drug by itself. That the doses as contained are minimal and effective is distinctly advantageous.

The alkaline carbonates are in Carminzym in stated quantities; the physician adjusts the dosage to the individual patient and with obvious evidence of the efficiency of the adjustment. As we understand it, the employment of alkaline carbonates is not based on purely chemic considerations—a definite known quantity of acid of the gastric juice is to be neutralized; the whole literature and practice dealing with the alkaline carbonates show them to be accredited with a much wider field of use and repute in gastro-intestinal disorders.

The pancreatic extract in Carminzym is designed to be diffusible in the stomach, the tablet is preferable to be crushed in the mouth before swallowing, and we believe the pancreatic extract to be an effective constituent as administered in Carminzym.

You comment as follows:

> "Ipecac has a well defined though limited field of usefulness. When it is used it should be given with due regard to the amount needed by the patient and the frequency of the repetition of the dose."

This in a sense may be said of any of the most useful drugs, but not in the least special degree does it apply to ipecac, which is, on the contrary, of quite characteristic, peculiar range of therapeutic properties, useful in varying combinations and in widely varying proportions and doses according to the purpose for which it is employed.

Ipecac in well known official alkaline, carminative, laxative preparations occurs in the "average dose" in the varying qantities of 1/14, 1/10, 1/8 and 3/16 of a grain.

The ipecac in combination with the other ingredients in Carminzym is designed for a tablet which shall carry a minimal quantity whilst capable of adequate remedial action, thus admitting of increase of dosage or repetition as occasion requires. This quantity of ipecac was not taken at random, but chosen after long trial and consideration.

We believe that Carminzym possesses carminative properties in a superior degree and that, furthermore, in consequence of its composition it directly stimulates the gland secretions and thus exerts a beneficial action upon the whole digestive functions.

Carminzym is for use as occasion requires, and this is to be especially noted. Thus it is not only of direct benefit, but helpful in promoting systematic therapeutic measures and regimen.

The Council takes the ground that complex mixtures of remedial agents are so wrong that there is no longer warrant for their admission into New and Nonofficial Remedies; and that Carminzym is an irrational mixture.

We hold that certain desirable therapeutic properties may rationally be attributable to Carminzym; and that these are manifested in practice.

During the time since the description was sent and the receipt of the statement of the action of the Council, some ten months, Carminzym has proved of constantly increasing service.

The statement in the letter of Fairchild Bros. and Foster "The long established custom of the use of mixtures of remedial agents rests on considerations well known and generally accepted" might well be paraphrased to read: The one-time prevalent custom of using ill-considered combinations of remedial agents has been thoroughly discredited and is generally abandoned by progressive practitioners. Such argu-

ments as that "laxatives, tonics, carminatives, diuretics are combined with distinct advantage" have led to the use of irrational mixtures such as the compound syrup of hypophosphites and the electuary of theriaca. The Council is confident that no one who has studied the causes and treatment of digestive disorders will find occasion to prescribe at one time all the ingredients stated to be contained in Carminzym, and certainly not in the fixed proportions present therein.

The comments in the Council's report concerning ipecac certainly does apply to all active therapeutic agents. Ipecac was mentioned in the report because the several constituents of Carminzym were under discussion and hence it was necessary to point out the futility of the small dosage of ipecac in this mixture.

The announcement that "Carminzym has proved of constantly increasing service" is not convincing. The Council does not know of a single clinical study of the action of Carminzym under conditions which would have afforded satisfactory evidence of its therapeutic value.

PHILLIPS' PHOSPHO-MURIATE OF QUININE COMP.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Oct. 19, 1918, p. 1335

The following report on Phillips' Phospho-Muriate of Quinine Comp. has been adopted by the Council and authorized for publication.

W. A. Puckner, Secretary.

Phillips' Phospho-Muriate of Quinine Comp.[1] is sold by the Charles H. Phillips Chemical Co., New York. According to the published formula, each fluidrachm contains:

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1. The evolution of "Phillips' Phospho-Muriate of Quinine Comp." from "Phillips' Wheat Phosphates" may be interesting. Every one knows that therapeutics tends to fashions, and "Phillips' Wheat Phosphates" appears to have had its inception as the result of the observation that super-refined white flour contains less phosphates than the corresponding amount of wheat. It was assumed that such flour must be deficient in an essential constituent, and the Wheat Phosphates preparation was apparently designed to fill the want. It was exploited for the relief of numerous conditions that were supposed, without satisfactory evidence, to result from this deficiency. When iron, quinin and strychnin mixtures became the vogue a quarter of a century ago, it was only natural to ride on the wave of popularity and the already widely advertised "Wheat Phosphates" was further enhanced—commercially—by the addition of the iron, quinin and strychnin, the amount of alkaloid added being practically negligible. Those who are not familiar with the various phases of the phosphorus, phosphoric acid, lactophosphate, lecithin, nuclein and glycerophosphate propaganda are referred to a report of the Council on Pharmacy and Chemistry in The Journal A. M. A., Sept. 30, 1916, p. 1033.

Phosphoric Acid	2 minims.
Potassium Phosphate, Magnesium Phosphate, Calcium Phosphate, Ferric Phosphate	2¼ grains
Quinin Muriate (equal to nearly ½ gr. Bi-Sulph.)	¼ grain
Strychnin	1/120 grain
Flavoring, Glycerin and Syrup, *q. s.*	

Some typical claims made for the preparation are:

"With marked beneficial action upon the nervous system. To be relied on where a deficiency of the phosphates is evident."

". . . brace those tired nerves and aid that worn stomach with Phillips' Phospho-Muriate of Quinine."

"The maintenance of a satisfactory blood pressure level free from intervals of depression may be accomplished by the use of Phillips' Phospho-Muriate of Quinine Compound in appropriate doses."

"The quantities of quinin and strychnin in this preparation are so well balanced that they relieve the depression and fatigue from mental or physical exertion, without the necessity of recourse to alcoholic stimulation."

"The other ingredients of Phillips' Phospho-Muriate of Quinine—phosphoric acid, and the phosphates of potash, magnesia, lime, and iron—are the most rational as well as convenient means of administering these tissue remedies, and of introducing phosphorus—the vitalizing constituent of the nervous system—into the organism."

The action of such a mixture as a whole is practically that of the sum of the actions of its constituents. The therapeutic action of strychnin and quinin are described in every text-book of therapeutics, but it is necessary to distinguish carefully between the various conditions in which these alkaloids have been used without discrimination, and those conditions in which they have been proved to be of value. While both have been widely used in a great variety of conditions, neither is of proved value in more than a distinctly limited range of diseases. The manufacturers of Phillips' Phospho-Muriate of Quinine Comp. seem to appeal to the less discriminating who use these alkaloids without any definite conception of exactly what they seek to accomplish with them. Quinin, although used by the uncritical in a host of diseases, has a definite field of usefulness in the treatment of malaria, both prophylactic and curative, but the required dose in the treatment of malaria is many times larger than that recommended in the Phillips' preparation. The claim that the "strychnin and quinin in this preparation are so well balanced that they produce a mild, buoyant effect, so advantageous, instead of alcoholic stimulation, to relieve depression and fatigue from mental or physical exertion" is nonsensical, if, indeed, it is not mendacious balderdash.

Calcium and potassium have important functions in the body, but any deficiency that may arise is usually attributable

to an inability of the body to utilize that which is supplied, for there is seldom any deficiency of these salts in the food, and when they are needed they are best supplied as simple solutions of the salts in appropriate doses without all of the other constituents of Phillips' Phospho-Muriate of Quinine Comp.

Phosphoric acid exerts practically the same actions as other mineral acids, hydrochloric being usually preferred for internal administration in certain forms of indigestion, aside from which they are seldom used as such.

In the more recent literature for Phillips' Phospho-Muriate of Quinine Comp., we find the attempt to utilize the well known craze about phosphorus, which has been through so many phases, every one of which has had its day and has been discarded.

The phosphoric acid and phosphates present in Phillips' Phospho-Muriate of Quinine are of no more value in nervous diseases than is simple sodium phosphate which does not require the addition of a host of other ingredients for its action. As a matter of fact, the phosphates of calcium and potassium present in a dose of Phillips' Phospho-Muriate of Quinine are probably devoid of appreciable effect in practically all conditions.

To pretend that one who suffers from physical and nervous exhaustion can be materially benefited by this mixture is sheer nonsense and is unworthy of a moment's consideration by a clinician who is called on to treat such patients.

Iron is useful in anemia, as every one knows. Iron has practically no other field of usefulness in therapeutics. When it is indicated it should be administered in a simple form, such as the pill of ferrous carbonate, for example, and not in a "shotgun" mixture that is quite as likely to do harm as good.

The claim that a satisfactory level of blood pressure can be maintained by Phillips' Phospho-Muriate of Quinine is mentioned only to condemn as the limit of impudent therapeutic claims. It is an insult to the intelligence of any practitioner to pretend that any known agent or combination of remedial agents can maintain a uniform blood pressure in any one of innumerable conditions.

In short, Phillips' Phospho-Muriate of Quinine Comp. is a complex and irrational mixture exploited by means of unwarranted claims. It is a survival of the old days of therapeutic chaos when impossible and fantastic chemical formulas were gravely published and as solemnly accepted without question, and also without the slightest understand-

ing on the part of many; when the most eminent of practitioners did not hesitate to give glowing testimonials for lithia waters that contained no more lithium than ordinary river water; when no therapeutic claim was too preposterous to receive acceptance, no theory too nonsensical to justify the use of all manner of claptrap mixtures for all manner of conditions.

EMETIN BISMUTH IODID ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Dec. 14, 1918, p. 2013

The Council has voted to accept emetin bismuth iodid for New and Nonofficial Remedies and to include Emetin Bismuth Iodid-Abbott and Bismuth Emetin Iodid-Mulford as accepted brands. It has authorized publication of the following report on emetin bismuth iodid.

W. A. PUCKNER, Secretary.

Historical: Emetin bismuthous iodid was introduced by A. G. DuMez in 1910. It varies considerably in composition according to its preparation. The sample analyzed by DuMez contained about 29 per cent. of emetin. The compound is insoluble in water and dilute acids, but is decomposed by alkalis. On the basis of these solubility characters, DuMez in 1910 suggested that it should pass the stomach unchanged, and thus have a lesser tendency to produce vomiting and diarrhea; but that it would presumably be decomposed and absorbed in the alkaline intestines.

DuMez did not have any clinical trials made, and his suggestion was neglected, until it was revived by Dale in 1916. Dale took up the subject because of the unsatisfactory results from the hypodermic emetin treatment in chronic cases, and carriers, of amebic dysentery. He assumed that the intestinal ameba at least might be reached more directly by oral administration than by the circulation. He therefore prompted the clinical trial of the DuMez compound, with promising results.

Administration: Dale employed a dosage of 3 grains of emetin bismuth iodid (corresponding to about 1 grain of emetin) daily, for 12 days. This dosage has been followed by subsequent observers. Dale gave the daily quotum at a single dose, during or after a full meal. Some of the others have given it in divided doses, and at different times. Apparently the midday meal is best, since the after-effects then cause the least inconvenience.

Dale also suggested a keratin-coated pill. As the coating of pills with keratin is now generally recognized to be of little value as a means of preventing the disintegration of pills by the gastric juice (Reports Coun. Pharm. & Chem., 1911, p. 58) salol-coated pills or capsules should be tried and also the wax mass proposed by N. S. Davis (THE JOURNAL, Oct. 14, 1916, p. 1160) and the procedure of Ballenger and Elder (THE JOURNAL, Jan. 17, 1914, p. 197).

Efficiency: All the clinical observers report satisfactory results. The disappearance of amebas from the stools is generally complete and apparently permanent even in chronic cases and carriers, and in patients in whose cases the hypodermic injections had failed. The compilation of Waddell and co-workers (1917) is most comprehensive. It shows about 18 per cent. of failures in carriers. This may be considered an excellent showing. The method in acute cases also is at least equal to the hypodermic administration of emetin hydrochlorid.

Side-Actions: The statements in regard to these vary somewhat, as might be expected. It is clear, however, that the preparation is far from nonirritant and produces much more gastro-intestinal disturbance than does the hypodermic method. Waddell *et al.* report that practically all patients respond either by purging or vomiting or both; the two phenomena being generally of inverse severity.

Low and Dobell state that "some of these [symptoms] recall to one's memory the old ipecacuanha days," although the symptoms are generally not quite so severe. Unfortunately there are no published records of parallel observations on the severity of these symptoms, comparing the plain ipecac treatment, by Simon's method for instance, with the emetin-bismuth compound and with the adsorption preparation ("Alkresta Ipecac").

Waddell *et al.* state that the vomiting starts in about one hour, the diarrhea in three hours. They can be checked only by opiates. Practically no tolerance is acquired. The vomitus generally has the red color of the drug, showing that the keratin coating had dissolved in the stomach. Evidently this confers but little protection. The severity of the nausea and vomiting varies considerably for different patients. This variation is not to be accounted for by variations in the drug, for this was of the same origin in most of the series. Presumably the variable reaction of the stomach may be an important factor in gastric solution and local irritation by the drug. However, it must be remembered that the emesis is largely of central origin (Eggleston and Hatcher, 1915),

and therefore could not be avoided by any method that would permit the absorption of the emetin.

Evidently, the side-effects of the drug are still very undesirable, although they do not preclude its use and are less disagreeable than with the old methods of oral administration. In view of the distinct field of usefulness for the oral method from the standpoint of efficiency and convenience, the emetin bismuth iodid preparations have been accepted for New and Nonofficial Remedies.[1] It is desirable that further methods of insuring gastric insolubility be sought. It is also worth while to determine if smaller daily doses may not perhaps be efficient.

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THE QUALITY OF THE MARKET SUPPLY OF PROCAINE

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 11, 1919, p. 136

The following report has been authorized for publication by the Council. W. A. Puckner, Secretary.

In accordance with its announcement (The Journal, Sept. 22, 1917, p. 1018) to report from time to time on the quality of American-made synthetic drugs, an examination of the market supply of procaine has been made. As explained at the time, the control of synthetic drugs, which, as a result of the war, are now made in this country, is in the furtherance of American industry, for the protection of the public, and in the interest of physicians. Since the manufacture of this class of drugs is to some extent experimental in this country, it is due physicians and the public that they be given the protection which will come from an investigation of the market supply. In view of the occasional reports of accidents with local anesthetics, an examination of the market supply of procaine was deemed particularly desirable. Hence, the A. M. A. Chemical Laboratory was asked to report if the product now offered for sale was satisfactory from a chemical

standpoint while the aid of the Pharmacologic Laboratory of Cornell University Medical School was invoked to determine if any of the product was unduly toxic.

Procaine, which chemically is the mono-hydrochloride of Para-amino-benzoyldiethyl-amino-ethanol, is the non-proprietary name selected by the Federal Trade Commission as the official designation for the drug previously known under the proprietary name "novocaine." Before the war procaine was obtainable in this country only through the Farbwerke Hoechst Co., the American representative of the German establishment, Farbwerke, vorm, Meister, Lucius and Bruening, under the name "novocaine." This monopoly on "novocaine" was exercised by virtue of United States patent No. 812,554, which was issued to Alfred Einhorn, Munich, Germany, assignor to Farbwerke, vorm, Meister, Lucius and Bruening, Hoechst a. M., in 1906. With the outbreak of hostilities, Congress passed the Trading with the Enemy Act, and under this, the Federal Trade Commission took charge of the novocaine patent with a view of securing the production of this product in the United States. To ensure an adequate supply of the drug, the Federal Trade Commission on recommendation of the Committee on Synthetic Drugs of the National Research Council, in addition to issuing a license to the Farbwerke Hoechst Company (which license was later transferred to the H. A. Metz Laboratories) granted authority to the Abbott Laboratories and the Rector Chemical Company to manufacture it under the U. S. patent after specimens submitted by these firms had been found satisfactory in the Association's Laboratory and at the Cornell Pharmacologic Laboratory.

After the three licenses had been issued, the Council examined specimens which each of these firms submitted as representing the market supply. These were found satisfactory and the preparations being marketed in conformity with its rules, the Council admitted procaine-Abbott, procaine-Farbwerke (novocaine), and procaine-Rector to New and Nonofficial Remedies as brands of procaine.

To obtain specimens representing the market supply, orders for the three brands of procaine were recently placed with pharmaceutical firms in New York, Baltimore and San Francisco. The Baltimore and San Francisco firms supplied specimens of procaine-novocaine brand and procaine-Rector brand but reported that the Abbott brand was not procurable. The New York correspondent was able to supply procaine-Rector only. As the entire output of the Abbott Laboratories was stated to go to the Government, specimens of this product were obtained through the Surgeon-General

of the Army from the General Purchasing Office, Medical Dept., U. S. Army. The following specimens were obtained and examined:

1. Procaine-Abbott, 6 specimens: The first specimen bore no serial number but the five later specimens were designated respectively, No. 89999, No. 89998, No. 89997, No. 89996, and No. 810995 representing batches from which shipments are to be made on contracts placed by the General Purchasing Office, Medical Department, U. S. Army, with the Abbott Laboratories of Chicago.

2. Procaine-novocaine brand, 4 specimens: These were designated respectively, A56, A57, A63, and A67. The first two specimens were labeled "Manufactured by the Farbwerke-Hoechst Co. at the H. A. Metz Laboratories." The third specimen (not in original container) was labeled "H. A. Metz Laboratories" and the fourth was marked "Manufactured by the H. A. Metz Laboratories."

3. Procaine-Rector, 3 specimens: Each bore the statement "Manufactured by the Rector Chemical Company" but had no "lot number."

Report of the A. M. A. Chemical Laboratory

To determine the quality of procaine now offered to the medical profession, the several specimens of each brand which had been purchased were submitted to the tests employed when specimens were previously examined for the Subcommittee on Synthetic Drugs of the National Research Council, and for the Council on Pharmacy and Chemistry. These tests were essentially those of New and Nonofficial Remedies and of the German Pharmacopoeia; it is, of course, not in the U. S. Pharmacopoeia. They require that the specimens shall respond to tests of identity for procaine (para-amino-benzoyldiethyl-amino-ethanol-hydrochloride); shall be odorless and colorless crystals or crystalline powder; shall melt at 153 to 155 C.;[1] shall be free from metallic impurities, and readily carbonizable matter, and on incineration leave not more than 0.1 per cent. ash.

In the accompanying table the results of the examination are given. For comparison the findings for the specimens examined previously are included.

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1. U. S. patent number 812,554—the novocain patent—declares that the salt melts at 156 C. Evidently based on this, both the German Pharmacopoeia and New and Nonofficial Remedies give this melting point. Two specimens of German made novocain obtained from our files, stated to be manufactured by Farbwerke-Hoechst vorm. Meister, Lucius, and Bruening, Hoechst a.M. were found to melt respectively between 154 and 155 C. and between 153.5 and 154.5 C. when the melting point was determined according to the directions of the U. S. Pharmacopoeia, 9th revision. The various specimens examined at that time melted between 153 and 155 C. and it was decided to permit this range.

From this examination it appears that all the specimens of procaine received complied satisfactorily with all tests of identity and purity with the following exceptions: (1) One specimen of procaine-Abbott had a melting point slightly below the permitted range; however, the last five specimens had the required melting point. (2) Five specimens of procaine-Abbott and the last three specimens of procaine-Rector were not entirely colorless, but had a yellow or light brown tinge.

Report from the Cornell Pharmacologic Laboratory

The following is the report of the toxicity determinations carried out on the specimens of procaine above enumerated, in the Pharmacologic Laboratory of Cornell University, Medical School, by Dr. R. A. Hatcher with the assistance of Dr. C. Eggleston.

Because of the serious or even fatal accidents occasionally reported from the use of local anesthetics (The Journal, Jan. 26, 1918, p. 258), it was thought prudent to determine that specimens of procaine should not be unduly toxic under normal conditions. Such tests have been made for the Subcommittee on Synthetic Drugs when the issuance of licenses for the manufacture was under consideration and have been a prerequisite to the acceptance for New and Nonofficial Remedies.

Twenty-five milligrams of drug per kilogram weight of cat in 5 per cent. solution is injected intravenously, and after 15 minutes, the same amount is again given in the same way. The dose administered in the test corresponds to over 1.5 gm. of drug for an adult of average weight administered intravenously, by which route the toxicity of the drug is far greater (approximately ten times as great) than by the subcutaneous method ordinarily used in clinical practice.

When the several market specimens of procaine were tested in this way, the animals so tested succumbed in no case. These results indicate that none of the specimens is to be considered dangerous when used in ordinary dosage for normal individuals. (Since the accidents attending the use of procaine depend on abnormal conditions not understood at present, no responsibility for the safety of the drug can be assumed as a result of these experiments.)

Several specimens of procaine-Rector and five of procaine-Abbott are decidedly brownish in color even when finely powdered and yield yellowish solutions.[1] All the earlier specimens from the Abbott Laboratories and from the Rector Chemical Company were beautifully white and crystalline.

1. A specimen of procaine recently sent the Council by the Metz Laboratories had a faint tinge of yellow, but, like the discolored Rector and Abbott specimens, complied with the identity and purity tests for procaine.

Brand	Date Received	Color	Melting Point	Ash
Procain (Abbott), from Committee on Synthetic Drugs....	12/21/17	White	154-155 C.	None
Procain (Abbott), submitted to Council P. and C.	1/29/18	White	153.5-154.5 C.	None
Procain (Abbott), Gen. Pur. Off. U. S. Army.....	8/31/18	White	152.5-153.5 C.	None
Procain (Abbott), Gen. Pur. Off. U. S. Army, No. 89999.....	9/30/18	Slight brownish tint	153-154.5 C.	None
Procain (Abbott), Gen. Pur. Off. U. S. Army, No. 89998.....	9/30/18	Slight brownish tint	153-154.5 C.	0.005%
Procain (Abbott), Gen. Pur. Off. U. S. Army, No. 89997.....	10/ 8/18	Slight brownish tint	153-154 C.	None
Procain (Abbott), Gen. Pur. Off. U. S. Army, No. 89996.....	11/ 4/18	Slight brownish tint	153.5-154.5 C.	None
Procain (Abbott), Gen. Pur. Off. U. S. Army, No. 810995....	11/ 4/18	Slight brownish tint	153.5-154.5 C.	None
Procain (Farbwerke Hoechst Co.), submitted to Council....	10/24/17	White	153-154 C.	None
Procain (Farbwerke Hoechst Co.), submitted to Council....	12/10/17	White	153-154.5 C.	None
Procain (Farbwerke Hoechst Co.), submitted to Council, market spec. "A56".....	8/ 9/18	White	153.5-154.5 C.	None
Procain (Farbwerke Hoechst Co.), submitted to Council, market spec. "A57".....	9/ 9/18	White	153.5-154.5 C.	None
Procain (H. A. Metz Lab.), market spec. "A63".....	8/23/18	White	153-154 C.	None
Procain (H. A. Metz Lab.), market spec. "A67".....	9/23/18	White	153-154 C.	0.018%
Procain (Rector), from Com. on Synthetic Drugs.....	12/18/17	White	153-154.5 C.	None
Procain (Rector), market spec.	8/20/18	Slight brownish tint	153-155 C.	None
Procain (Rector), market spec.	8/23/18	Slight brownish tint	153-155 C.	None
Procain (Rector), market spec.	8/23/18	Slight brownish tint	153-154.5 C.	None

The following tests were also made: About 0.01 to 0.02 gm. procaine was added to about 10 to 15 c.c. distilled water contained in a test tube, and this placed in a bath of boiling water for one hour. The solutions were then cooled and examined. After standing over night, they were examined again. No deposit of any sort and no change of color could be detected in any case.

When the matter of the discolored specimens of procaine was referred to the Rector Chemical Company for explana-

tion, the firm wrote that some months ago for a short time for some unexplainable reason its procaine was slightly yellowish in color, but that every batch was carefully tested and found to answer all chemical requirements. The firm stated that the product which it has sent out for some time past has been white and yields a colorless solution.

To a like inquiry the Abbott Laboratories replied that the five samples which were found discolored were products manufactured by the Rector Chemical Company and represented goods which it had purchased to assist in filling delayed orders, because the firm had found itself unable to keep pace with the demand on account of delay in securing needed apparatus. The firm submitted protocols to show that the procaine made by it, by Rector and by Metz were of equal toxicity.

So far as the evidence goes, there is nothing to indicate that the yellowish or brownish colored specimens of procaine are seriously impure. On the contrary, the compliance with the chemical and toxicologic tests indicates that the color is due to an insignificant trace of some colored substance produced in the manufacturing process. In view of this, the Council considers the use of the discolored product to be justified in the present emergency, although it would urge that for the future the supply of procaine should be free from color and also comply to the tests of purity. It makes this request in the interest of the medical and dental professions, which use the drug, and also in a desire that in the manufacture of synthetic drugs, the United States shall occupy a high place.

"PLURIGLANDULAR" MIXTURES

Caps. Adreno-Spermin Comp., Caps. Antero-Pituitary Comp., Caps. Placento-Mammary Comp., Caps. Thyro-Ovarian Comp., Caps. Hepato-Splenic Comp., Caps. Pancreas Comp., and Caps. Thyroid Comp., Not Admitted to N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 18, 1919, p. 213

After considering the evidence for the several "pluriglandular" mixtures described below, the Council declared them inadmissible to New and Nonofficial Remedies. The Council's action was communicated to the manufacturer, Henry R. Harrower, in accordance with the usual procedure. After

giving due consideration to the manufacturer's reply the Council authorized publication of the report which appears below. W. A. PUCKNER, Secretary.

With the offer "to supply you with as much literature as may be necessary and as little of the actual remedies as may be desired" if "the prospects for the inclusion of these formulas in N. N. R. are good," Henry R. Harrower sent the Council a booklet descriptive of his preparations and labels for the following mixtures:

Caps. Adreno-Spermin Comp., each said to contain "Adrenal Gland (total) gr. ¼, Thyroid Gland (U. S. P.) gr. 1/12, Spermin Extr. (from Gonads), Brain and Spinal Cord aa gr. 1, Calc. Glycerophosphate q. s. ad gr. 5."

Caps. Antero-Pituitary Comp., each said to contain "Anterior Pituitary Body gr. 2, Thymus Gland gr. 1, Thyroid Gland (U. S. P.) gr. 1/12, Calcium-phosphorus Comp. q. s. ad gr. 5."

Caps. Placento-Mammary Co., each said to contain "Desiccated Placenta gr. 2, Mammary Substance gr. 1½, Pituitary Body (total) gr. ⅓, Calcium-phosphorus Comp. q. s. ad gr. 5."

Caps. Thyro-Ovarian Comp., each said to contain "Desic. Corpora Lutea Ovarian Substance gr. 2½, Thyroid Gland (U. S. P.) gr. 1/12, Pituitary Gland (total) gr. ⅛, Calcium-phosphorus Comp. q. s. ad gr. 5."

Caps. Hepato-Splenic Comp., each said to contain "Liver Parenchyma, Spleen Substance aa gr. 2, Powd. Bile Salts gr. ½, Adreno-Spermin Co. (No. 1) gr. 1."

Caps. Pancreas Comp., each said to contain "Adrenal Gland, Pituitary Gland (total) aa gr. ½, Ovarian Substance gr. 1, Pancreas Substance q. s. ad gr. 5."

Caps. Thyroid Comp., each said to contain "Desic. Thyroid Gland (U. S. P.) gr. ⅛, Calcium-phosphorus Comp. q. s. ad gr. 5."

The Council declared these preparations inadmissible to New and Nonofficial Remedies, for reasons which follow:

1. Each of the mixtures contains one ingredient or more, which is neither recognized in the U. S. Pharmacopeia nor admitted to New and Nonofficial Remedies, namely: "Spermin Extract," "Brain," "Spinal Cord," "Desiccated Placenta," "Liver Parenchyma," "Spleen Substance," "Pancreas Substance" and "Calcium Phosphorus Comp. (Each 100 gm. represents Magnes. Phos. 1; Calc. glycerophos. 4; Potas. bicarb. 15; Sod. bicarb. 22 and Sod. chlor. q. s.)." For obvious reasons the Council does not accept a mixture containing an indefinite ingredient and hence it would be necessary as a preliminary for the consideration of any one of the mixtures that their unofficial ingredients be made eligible for New and Nonofficial Remedies by the submission of evidence that such ingredient is of uniform composition and that it is therapeutically valuable when given by mouth. There is no evidence that many of these organs have any value whatever when administered by the mouth or in any other way.

2. In the light of our knowledge the administration of gland mixtures in the host of conditions enumerated in the advertising circular is irrational and on a par with the use of the shotgun mixtures once in vogue.

Be it a pharmaceutical mixture, a "mixed" vaccine, or a "pluriglandular" product, the combination of two medicinal ingredients in a mixture must be considered contrary to rational therapy unless a good reason exists for such combination. Such mixtures are held in conflict with Rule 10 unless the manufacturer presents acceptable evidence for the value of his combination. A physician may prescribe any mixture which he considers indicated in a given case, but the marketing of mixtures of drugs in fixed proportions is in most instances irrational and a detriment to sound therapy.

B. IODINE AND B. OLEUM IODINE

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Feb. 1, 1919, p. 365

The Council has authorized publication of the following report on "B. Iodine" and "B. Oleum Iodine" together with the reply submitted by the manufacturer and a discussion thereon by the referee in charge of the preparations.

W. A. Puckner, Secretary.

Specimens of B. Iodine and B. Oleum Iodine (B. Iodine Chemical Company) and an advertising pamphlet were sent to the Council by John Bohlander, A.M., M.D., with the declaration:

"Well knowing the value of Iodin in surgical operations and dressings, prompted me for the benefit of my fellow physicians as well as myself, and for Humanity's sake, to make Iodin my master-piece in chemistry.

"After several years of diligent work in my private laboratory I succeeded in discovering a new product of Iodin—Nitrogen, hydrate of Iodin."

While "B. Iodine" is said to be nitrogen hydrate of iodin and "B. Oleum Iodine" a 5 per cent. solution thereof, the examination made by Prof. A. H. Clark of the University of Illinois, School of Pharmacy (working in the A. M. A. Chemical Laboratory), indicates that the first is a simple mixture of iodin and ammonium iodid, and the second a solution of iodin in liquid petrolatum. The Council adopted the report of the A. M. A. Chemical Laboratory (which appears below) and declared B. Iodine and B. Oleum Iodine inadmissible to New and Nonofficial Remedies because:

1. The composition is incorrectly declared. B. Iodine is not a newly discovered iodin compound, "Nitrogen Hydrate of Iodine," but a mixture of iodin and ammonium iodid. B. Oleum Iodine is not a 5 per cent. solution of B. Iodine as suggested by the statement on the label and in the advertising, but a solution of iodin in liquid petrolatum containing about 0.85 per cent. of iodin.

2. Since B. Iodine is a mixture of iodin and ammonium iodid, its solution in water will have the properties of other solutions of iodin made by the aid of iodid, such as a dilution of tincture of iodin or of compound solution of iodin (Lugol's solution). Hence, the therapeutic claim that B. Iodine "being of a colloidial nature has the advantage of being more readily absorbed and taken up by all cellular structure, thus getting a perfect cellular medication of Iodine," is unwarranted.

3. The names "B. Iodine" and "B. Oleum Iodine" are not descriptive of the pharmaceutical mixtures to which they are applied.

4. B. Iodine and B. Oleum Iodine are unessential modifications of established articles. B. Iodine has no advantage over tincture of iodin or compound solution of iodin. (As more convenient of transportation, the Medical Department of the U. S. Army supplies its field hospitals with a mixture of iodin and iodid ready for solution in water, either in tablet form or in powdered form in tubes.) Solutions of iodin in liquid petrolatum may be readily prepared (Reports Council Pharm. and Chem., 1917, p. 88).

[Contribution from the A. M. A. Chemical Laboratory]

B. IODINE PRODUCTS

A. H. Clark, Ph.G., B.S.

"B. Iodine" products are marketed by the B. Iodine Chemical Company, Cincinnati, Ohio; John Bohlander, A M., M.D., is said to be the discoverer. They consist of "B. Iodine," "B. Oleum Iodine," and "B. Aqua Iodine." B. Iodine and B. Oleum Iodine were submitted to the Council.

In a circular submitted by the B. Iodine Chemical Company, B. Iodine is said to be "Nitrogen Hydrate of Iodin." It is claimed that "coming in contact with water, H_2O, a chemical change takes place forming Hydro Oxid of Iodin, the Nitrogen of the Nitrogen Hydrate of Iodin escaping, the balance taking up one of oxygen of the water. Its companion, the H_2, escaping at the same time with the Nitrogen then combining with the remainder of the water to form the solution of Hydrogen Oxid of Iodin; so you can readily see that you really have a pure water of Iodin, nothing but the H, the O and the I."

B. IODINE

According to the circular, B. Iodine is soluble in alcohol, chloroform, and ether. Also it:

"Has odor, taste, melting and boiling point, same as regular Iodin, has a great affinity for water and will respond to all the tests of Iodin. Appears in a Bluish Black Granulated mass or powder. When heated in vaporating dish will throw off large purple volumes of Iodin leaving a slight white crystaline precipitate, which on continuous heating will entirely disappear. With careful manipulation you can get prismatic needle point like crystals, looking like spores of glass, these dissolving in water will yield pure Iodin coloring the water Iodin.

"PHARMACOLOGIC, THERAPEUTICAL AND PHYSIOLOGICAL ACTION: Same as Iodin, being of a colloidal nature has the advantage of being more readily absorbed and taken up by all cellular structure, thus getting a perfect cellular medication of Iodin."

A sample of B. Iodine, marked "Nitrogen Hydrate of Iodin" was submitted by the manufacturers and this sample was examined.

B. Iodine was found to be a granular powder, almost black with a purple cast. It has an odor of iodin and dissolves in water readily. It is also quite soluble in alcohol, but not entirely soluble in chloroform and ether. Ether quickly dissolves iodin from B. Iodine leaving a residue of a white granular substance. Chloroform acts the same as ether except that the iodin is dissolved out with some difficulty. On heating B. Iodine, vapors of iodin escape. If the heating is done on a water bath, a residue of a white granular substance, subsequently identified as ammonium iodid, remains. If heated in a bunsen flame, no residue remains. These tests all indicate that iodin is held in the form of a simple mixture.

Ammonia: B. Iodine when mixed with an excess of sodium hydroxid and warmed, evolves ammonia.

Iodine: 0.1567 gm. B. Iodine dissolved in water required 5.88 c.c. tenth-normal sodium thiosulphate solution indicating 48.28 per cent. iodin. 0.3721 gm. B. Iodine required 14.18 c.c. tenth-normal sodium thiosulphate solution indicating 48.37 per cent. iodin. The average is 48.33 per cent. iodin.

Ammonium Iodide: 0.3453 gm. of the residue after heating B. Iodine on a water bath until all iodin had volatilized was dissolved in water, acidulated with phosphoric acid, and hydrogen dioxid solution added. The liberated iodin was extracted with chloroform and titrated with tenth-normal sodium thiosulphate. 23.78 c.c. were required indicating 0.3447 gm., or 99.83 per cent., ammonium iodid.

A mixture of 5 gm. iodin and 5 gm. ammonium iodid has the properties of B. Iodine mentioned above.

The conclusion is that B. Iodine is essentially a mixture of iodin and ammonium iodid in equal parts, the two substances being finely powdered and intimately mixed.

B. OLEUM IODINE

The following regarding B. Oleum Iodine is quoted from the circular submitted:

"B. .OLEUM IODINE: Iodine soluble in mineral oil 5 and 10% for Nasel, Pharyngeal, Laryngeal, Bronchial, Rectal, etc., and all meucoid affections and abnormal conditions of the mucous membrane."

A sample of B. Oleum Iodine was submitted by the manufacturer and examined. The label on the bottle states that it is 5 per cent. B. Oleum Iodine in mineral oil. This sample has the characteristics of a solution of iodin in liquid petrolatum. It is oily and has the characteristic violet color.

Ammonia: B. Oleum Iodine, since it is presumed to be a solution of B. Iodine, was examined for ammonium compounds. A small quantity was mixed with an equal volume of strong sodium hydroxid solution and heated. No ammonia was evolved. A few crystals of ammonium chlorid were added to a little of B. Oleum Iodine and treated as above. Ammonia was readily detected.

Iodine: 5.255 gm. B. Oleum Iodine was dissolved in chloroform and placed in a separator. A solution of potassium iodid was added and the iodin titrated with tenth-normal sodium thiosulphate solution. It required 3.5 c.c. indicating 0.85 per cent. iodin.

The conclusion is that B. Oleum Iodine is a simple solution of iodin in liquid petrolatum to the extent of 0.85 per cent. and not 5 per cent. as claimed. Furthermore, it is not a solution of B. Iodine since no ammonium compound is present.

The preceding report was sent to the B. Iodine Chemical Company. The following reply was received:

Your letter of the 21st inst., received and contents noted and cannot quite agree with your report.

Reasons why: NH_4I, a Nitro Hydrate Iodide; NH_4I_2, a Nitro Hydrate Iodate; and $NH_4I_2I_2$, Per Iodide, a molecular compound, which I claim, they all being of a NH group, so what can be the objection of Nitrogen Hydrate of Iodine? Of course when your chemist, with the aid of heat, drove off all the Iodine, he naturally brought it back to a NH_4I. There's where he gets the A.M. I claim a molecular compound.

The Oil of Iodine I sent you by mistake was a 1 per cent. and not a 5 per cent. as marked. I claim it is made from the resublimed Iodine in mineral oil and not the B. Iodine. I claim a 5 per cent. has heretofore never been accomplished, so I therefore can claim something new.

Tr. Iodine contains Alcohol and Potash as a base, the alcohol a dehydrater and Potash an escharotic, and all other soluble Iodines like the tincture have a metallic base. Mine has not. My iodine is compatable almost with all the salts, alkaloids, tannates, and even the metals. You can't say that for the tincture or the others. Now why should mine not be superior to others?

Preparations as yet are not on the market and a few pamphlets were printed to meet with the requirements of your rulings and approval and shall be corrected if we only can agree on a proper name as you may suggest.

Yours very truly,

THE B. IODINE CHEMICAL CO.
By John Bohlander, A.M., M.D.

P. S. We are sending you under separate cover another sample of the Oil of Iodine which is a 5 per cent. solution, and allowing for deterioration will test at least four per cent.

The referee in charge of the preparations submitted the above letter to the Council with the following comments:

The principal statements in the letter are essentially erroneous or misleading: Mixtures or double salts of ammonium iodid and iodin were not discovered by Dr. Bohlander, and are nothing new. Watery solutions of iodin by means of an iodid have long been known and used in the form of Lugol's solution.

There is no evidence that ammonium iodid is less irritating than potassium iodid. On the contrary, ammonium salts are generally more irritating than the corresponding potassium salts. B. Iodine is not compatible with alkaloids, but behaves essentially like Lugol's solution. The A. M. A. Chemical Laboratory reports that the new sample of B. Oleum Iodine contains only 1.2 per cent. of free iodin, instead of the claimed amount. It is therefore somewhat weaker than the iodin petrolatum prepared by the A. M. A. Chemical Laboratory (Reports Council Pharm. and Chem., 1917, p. 88).

However good Dr. Bohlander's intentions may be, the statements that he makes about his products are misleading or erroneous, and the products are ineligible for N. N. R.

CERELENE NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Feb. 15, 1919, p. 513

The Council has authorized publication of the following report declaring Cerelene inadmissible to New and Non-official Remedies.

W. A. PUCKNER, Secretary.

Cerelene, a paraffin preparation for the treatment of burns, was submitted to the Council by the Holliday Laboratories, with the statement that it was composed of 84 per cent. paraffin, 15 per cent. myricyl palmitate, and 1 per cent. purified elemi gum to which is added oil of eucalyptus 2 per cent. and betanaphthol 0.25 per cent. It was explained:

> "Myricyl Palmitate is a purified form of Beeswax, free from all impurities, acids, etc., which is solely manufactured by this Company. . . ."

It was also stated that on "special order" Cerelene has been made containing oil of eucalyptus and resorcin, oil of eucalyptus and picric acid, and picric acid alone. The following report on the preparation was presented to the Council by the referee to whom Cerelene had been assigned:

Cerelene is another compound wax for the treatment of burns. According to the work of Sollmann (J. A. M. A., **68**:1799, 1917) it is highly improbable that compound mixtures have any advantage over simple paraffin of low melting point. Cerelene must therefore be considered as an unessential modification of paraffin, and as in conflict with Rule 10; unless definite evidence of superiority is submitted. Cerelene mixtures containing medicinal ingredients also appear unscientific since the evidence that the ingredients do not leave the wax has not been successfully contradicted. Finally, the claims made for Cerelene are rather extreme, and would need some revision before they could be accepted.

The A. M. A. Chemical Laboratory reports:

The physical properties of Cerelene are as follows:

Melting point 50.0 C. by U. S. P. method.
Ductility limit ..... 30.5 C.
Plasticity limit ..... 26.4 C.
Not strong at..... 38 C.

Adheres moderately well; detaches with "pulling." On heating, readily loses eucalyptol, and a small amount of resinous substance forms in the bottom of the beaker. If Cerelene is heated to 145 C. and cooled, the resulting product no longer has the properties of the original Cerelene.

It is recommended that the preceding report be sent to the Holliday Laboratories, and that unless its superiority over simple paraffins is demonstrated and the unwarranted claims abandoned, Cerelene be declared inadmissible to New and Nonofficial Remedies for conflict with Rules 6 and 10.

This report was submitted to the Holliday Laboratories with the information that it had been adopted, Oct. 3, 1917. It was also explained that before Cerelene could be accepted, the unofficial and unstandardized constituent "myricyl palmitate" would have to be considered and accepted for New and Nonofficial Remedies since, for obvious reasons, the Council does not accept a preparation which contains an unofficial and unstandardized substance not in N. N. R.

The Holliday Laboratories acknowledged receipt of the Council's report and asked that the matter be held in abeyance until the requested evidence had been obtained. Later the Council was advised that the advertising circulars for Cerelene had been withdrawn with the exception of one giving directions for its use. Five months later, the firm stated

that experiments were being made "to determine the actual strength of Cerelene in comparison with other paraffin waxes. . . ." Nothing further has been heard from the Holliday Laboratories and no reply has been received to an inquiry made Oct. 12, 1918. The Council therefore authorizes publication of its report declaring Cerelene inadmissible to New and Nonofficial Remedies.

ANTITHYROID PREPARATIONS (ANTITHYROIDIN-MOEBIUS AND THYREOIDECTIN) OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of antithyroid preparations (Antithyroidin-Moebius and Thyreoidectin) has been authorized for publication. W. A. PUCKNER, Secretary.

New and Nonofficial Remedies, 1918, contains a discussion of "antithyroid" preparations and describes two of these: Antithyroidin-Moebius (E. Merck, Darmstadt, Germany) and Thyreoidectin (Parke, Davis & Company, Detroit, Mich.).

The referee reported that these "antithyroid preparations" evidently have not realized the expectations of their promoters, and are viewed with skepticism by practically all critical clinicians.

Consequently, notwithstanding the cautiously worded statements of claims made by the manufacturers of Thyreoidectin, the Council approved the recommendation that this preparation (Thyreoidectin) be omitted from New and Nonofficial Remedies for conflict with Rule 6 (unwarranted therapeutic claims) and Rule 10 (unscientific and useless articles) (Antithyroidin-Moebius had already been omitted because it was off the market). The Council further directed that the general article "antithyroid preparations" be also omitted.

The Council having adopted the recommendation of the referee, Thyreoidectin is omitted from N. N. R., while the general article appears below, as a matter of record:

Antithyroid preparations are obtained from the blood or milk of animals, after the removal of the thyroid glands.

The use of these preparations is based on the theory that the thyroid gland secretes products which are toxic, but which neutralize, and are neutralized by, other toxic substances produced elsewhere in the body. Removal of the thyroid glands would then lead to the accumulation of these second toxic substances as evidenced by the phenomena of

cachexia strumipriva and myxedema. On the other hand, the blood or milk of such animals is claimed to be capable of preventing the effects of hypersecretion of thyroid substance, such as is supposed to occur in hyperthyroidism (Basedow's or Graves' disease—generally called exophthalmic goiter).

These views are largely hypothetical; attempts to give to them a rational experimental basis have failed, but some clinical observers report distinctly beneficial results in the milder forms of the diseases, and in obscure nervous disorders which are supposedly connected with thyroid hypersecretion from the administration of the milk from thyroidectomized goats and also from the use of the proprietary blood preparations listed below. The value of these preparations is very doubtful. The reported improvements may only be psychical or due to associated measures, as is often seen in this disease. Other measures of treatment should not be neglected.

Improvement is said to occur in two or three weeks and to be indicated by an amelioration of the nervous symptoms, tremor, palpitation, insomnia and excitability.

The administration must be long continued. Oral and hypodermic administration are said to be equally effective, but the former is usually preferred. These preparations are not known to be toxic, even when very large doses are used.

BORCHERDT'S MALT EXTRACT WITH ALTERATIVES

Report of the Council on Pharmacy and Chemistry

The following report was adopted by the Council and its publication authorized. W. A. Puckner, Secretary.

Borcherdt's Malt Extract with Alteratives (The Borcherdt Malt Extract Company, Chicago) was submitted to the Council with the claim that each fluidounce contained iodin, 1/30 grain; calcium iodid, 1 grain; potassium iodid, 2 grains, and calcium chlorid, 8 grains, in a vehicle of malt extract.

The preparation was declared inadmissible to New and Nonofficial Remedies:

1. Examination in the A. M. A. Chemical Laboratory disclosed that the article did not contain free iodin as claimed, that which was stated to have been added probably having combined with the proteins of the malt extract (Rule 1).

2. It being claimed that the preparation contained three forms of iodin (free iodin, potassium iodid and calcium iodid) and two forms of calcium (calcium chlorid and calcium iodid), the product is needlessly complex and therefore irrational (Rule 10).

3. The name of the preparation is not descriptive of its composition; in addition it is therapeutically suggestive (Rule 8).

CEPHAELIN AND SYRUP CEPHAELIN-LILLY OMITTED FROM N. N. R. AND SYRUP EMETIC-LILLY NOT ACCEPTED

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report, which explains the omission of cephaelin and Syrup Cephaelin-Lilly from New and Nonofficial Remedies and the non-acceptance of Syrup Emetic-Lilly.

W. A. PUCKNER, Secretary.

New and Nonofficial Remedies, 1918, describes cephaelin (an alkaloid obtained from ipecacuanha root) and lists Syrup Cephaelin-Lilly (containing 0.088 Gm. cephaelin hydrochlorid per 100 Cc.) as a pharmaceutical preparation of it.

The period of acceptance for Syrup Cephaelin-Lilly having expired, Eli Lilly & Company were asked to send the current advertising and labels so that the Council might determine if the acceptance of this preparation might be continued. In reply the firm wrote:

"We have changed the name of Syrup Cephaeline to Syrup Emetic but the product remains the same as before. We have no circulars describing Syrup Emetic and can only send copies of the label."

The new name "Syrup Emetic" conflicts with the rules of the Council in that it does not indicate the potent ingredient of this simple pharmaceutical preparation and in that it is therapeutically suggestive. Emetics are powerful agents, and physicians should be given every opportunity of knowing what they prescribe for the purpose.

The name being in conflict with Rule 8, the Council voted to omit Syrup Cephaelin-Lilly and not to accept Syrup Emetic-Lilly.

As the cephaelin syrup was the only preparation of cephaelin admitted to New and Nonofficial Remedies, and as the alkaloid appears to have no important therapeutic field, the Council directed that the description of cephaelin also be omitted.

COLALIN OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Colalin has been authorized for publication.

W. A. PUCKNER, Secretary.

Colalin is a bile salt preparation claimed to consist essentially of hyoglycocholic and hyotaurocholic acids. It is manufactured by Rufus Crowell and Company, Somerville, Mass.,, and marketed by Schieffelin and Company, New York.

An examination of the current advertising by the referee of the Council in charge of bile salt preparations having revealed that claims were made for Colalin which were not in harmony with the known action of bile preparations, Schieffelin and Company were informed that in the opinion of the referee the Colalin circular matter required radical revision. In this communication the referee's objections to the claims were set forth in detail.

No reply to this letter was received, and hence a copy of the letter was sent to Schieffelin and Company and also to Rufus Crowell and Company with the explanation that unless the statements in the Colalin advertising which the referee had questioned were substantiated by satisfactory evidence, were suitably revised, or else the advertising matter withdrawn pending revision, the referee would be obliged to recommend to the Council that Colalin be omitted from New and Nonofficial Remedies.

In reply, Schieffelin and Company wrote that they were not "engaged actively in the introduction of Colalin," and agreed to the omission of Colalin from N. N. R.

In view of the failure to substantiate the claims objected to or an agreement to discontinue them, the Council directed that Colalin and Colalin Tablets be omitted from New and Nonofficial Remedies for conflict with Rule 6 (unwarranted therapeutic claims).

The following are the claims which the referee questioned:

"Colalin embodies the physiological function of the bile in the intestinal canal and also possesses properties of its own which are intimately connected with the function of the liver."

The quotation implies that Colalin has properties essentially different from those of bile salts, a claim which requires substantiation.

"In the liver its action seems to be that of a general stimulant of all the hepatic functions."

This is a claim which requires substantiation.

"By the introduction of Colalin it has therefore become possible to actually utilize the bile for therapeutic purposes."

This is an unwarranted claim, for bile was used therapeutically before Colalin was introduced.

"As gall-stones are chiefly composed of cholesterin, experiments were made to determine whether Colalin would dissolve these concretions outside of the body. These were completely successful and were then followed by an extensive series of clinical investigations on persons suffering with cholelithiasis, which demonstrated that by the administra-

tion of Colalin in many instances gall-stones were evacuated by the natural passages and their further formation prevented without resort to surgical intervention."

This is misleading in that the context shows that "without surgical intervention" is meant to imply a connection between the experiments showing the solvent power of Colalin and the passage of concretions.

". . . Colalin not only acts as a solvent of cholesterin calculi, but prevents their further formation by removing the causes upon which their development depends."

This conveys the impression that such solvent action is exerted in the body, that is, that such concretions in the gallbladder may be dissolved and evacuated by the use of Colalin. For this claim there is no evidence.

"To understand the value of Colalin in intestinal disorders it is necessary to bear in mind the important functions of the bile in the intestinal canal, namely, its participation in the digestion of fats, its antitoxic action, and its influence upon the peristalsis."

". . . through its antiseptic influence inhibits the production of toxins in the intestines."

The referee believes that there is no satisfactory evidence that bile or bile salts can inhibit the production of toxins in that part of the intestine—the colon—in which they are commonly produced.

DIPHTHERIA BACILLUS VACCINE OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has directed that diphtheria bacillus vaccine be omitted from New and Nonofficial Remedies and authorized publication of the following report.

W. A. PUCKNER, Secretary.

The following description of diphtheria bacillus vaccine appears in New and Nonofficial Remedies, 1918, preceding that of the accepted brand, Diphtheria Bacterin-Mulford.

DIPHTHERIA BACILLUS VACCINE.—Made from *Bacillus diphtheriae.*

Actions and Uses.—Diphtheria bacillus vaccine has been used in the treatment of diphtheria bacilli carriers as a means of eliminating the bacilli which were resistant to other agents.

The Mulford Company informed the Council that it was no longer supplying diphtheria bacterin. Accordingly the Council directed the omission of the accepted brand and, as a matter of record, authorized publication of the preceding general description of diphtheria bacillus vaccine in the Annual Council Reports.

EMPYROFORM OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Empyroform has been authorized for publication. W. A. PUCKNER, Secretary.

Empyroform is a condensation product of birch tar and formaldehyde. It is manufactured by Chemische Fabrik auf Aktien, vorm. E. Schering, Berlin, German, and distributed in the United States by Schering and Glatz, Inc., New York.

The term of acceptance having expired, the Council voted to omit Empyroform because its usefulness is doubtful and the agents were not in a position to submit further evidence for its value at this time.

FORAL

Report of the Council on Pharmacy and Chemistry

The following report on Foral, a depilatory preparation, has been authorized for publication by the Council.

W. A. PUCKNER, Secretary.

Foral is sold by the Foral Products Company, Pittsburgh, Pa., as an "antiseptic depilatory" with the special claim for its use for the removal of hair prior to surgical operation or the dressing of wounds. In addition to claims made for its hair dissolving action, it is asserted that, in removing the hair from an open wound, Foral acts as "an antiseptic, which guarantees against any infection." It is also claimed that, though hair will return after its use, "by proper use it will diminish the growth of hair and cause the hair to grow much slower, and unlike the razor, the hair will not return coarser and thicker."

We are informed by the Foral Products Company that their preparation is used in many hospitals and that ". . . one and all are well pleased and a great satisfaction to do away with the old style razor. . . ."

Foral is stated to be made according to the following formula:

To manufacture seventy-five pounds of FORAL

Starch	35	pounds
Barium-Sulphide	20	pounds
Zinc-Oxide	10	pounds
Calcium-Carbonated-Precip	10	pounds
Potassium-Permanganate	10	grams
Menthol-Crystallized	10	grams
Carbolic-Acid	½	ounce
Lilac or Citronel oil	3	ounces

The four above chemicals are going to a heating process before mixing or sifting.

In consideration of the preceding, the Council declared Foral inadmissible to New and Nonofficial Remedies for conflict with its rules, thus:

1. Foral is an unessential and irrational modification of an established article.

While its manufacturer states that Foral has been on the market for eighteen years, the following depilatory formula appears in a book published thirty-five years ago (A Practical Treatise on Diseases of the Skin, Louis A. Duhring, Ed. 3, 1883) and is to be found in most books on dermatology:

Barium Sulphid	2 drams
Zinc oxid	3 drams
Starch	3 drams

Permanganates and sulphids mutually destroy each other, and therefore the addition of the small amount of potassium permanganate cannot serve any useful purpose. The amounts of phenol, menthol and "Lilac or Citronel oil" are too small to exercise any effect (other than that of a flavor) and must be considered unessential additions.

2. Foral is a pharmaceutical mixture marketed under a non-informing name.

Whereas it is in the interest of rational medicine that physicians should know the composition of the preparations which they use, the name of this pharmaceutical mixture fails to indicate that it contains the well-known and by no means always harmless barium sulphid.

3. Foral is sold under exaggerated and unwarranted claims.

In view of the small amount of phenol present and the method of using the preparation, the claim that the use of Foral which, when operating on open wounds, "guarantees against any infection," is evidently unwarranted.

There is no evidence for the claim that the use of depilatories such as Foral retards the growth of hair or renders hair less coarse. On the contrary, the commonly prevailing opinion is that depilation, like shaving, makes the hair coarser.

To determine if "one and all" of those who had used Foral were still using the preparation, four of the testimonials, appearing in an advertising pamphlet, were investigated. The pharmacist of the hospital from which the first of these testimonials was stated to have emanated replied that the person whose name appeared in connection with it had left the hospital about ten years ago and that no depilatory preparation has been used in this hospital for some time. So far as he knew, depilatories were not now in use in the surgical wards of the hospital. In regard to

the second testimonial, the pharmacist of this hospital wrote that the hospital had not bought the preparation, but that some of it had been obtained for an elderly deaconness, who had personal use for a depilatory. The physician signing the third testimonial replied that the preparation was effectual for the removal of hair from the scalp, but that ". . . we have gotten out of the habit of using it." In the case of the fourth testimonial, its asserted author wrote ". . . if it is applied in too large a quantity or too concentrated, or permitted to remain on too long, it will vesicate. It was for this reason chiefly that I discontinued its use. It is a very bad smelling mixture and patients complain of it very bitterly."

GLYCEROSAL

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report on Glycerosal. W. A. PUCKNER, Secretary.

Glycerosal (Röhm and Haas) is said to be a mixture of glyceryl salicylates prepared by heating methyl salicylate with glycerol. The mixture is to be used externally. It is claimed to be absorbed promptly, and to have a prolonged action without producing irritation of the skin and without affecting the digestive organs.

A dilute alcoholic solution is protected by the registered trade name "Antirheumol," but the manufacturers stated to the Council that it will not be marketed in this form and under this name.

There are already so many salicylic compounds available that a further multiplication tends to useless complication and confusion and discourages accurate acquaintance with the effects of the individual drugs. The introduction of further salicyl compounds is therefore undesirable, unless they be shown to have distinct advantages over the established drugs.

The advantages claimed for Glycerosal were not substantiated by satisfactory evidence. The claim that Glycerosal does not affect the digestive organs is certainly misleading since this would merely mean an insufficient dosage. Nausea is produced by adequate doses of salicylates, independent of the method of administration, since this action is chiefly central.

No satisfactory evidence for the superiority of Glycerosal over other salicylates having been submitted, the Council postponed its consideration to permit the manufacturer to ascertain if its absorption is better or its action more pro-

longed, or if it produces less irritation of the skin than do other salicylic acid esters, such as methyl salicylate, spirosal, etc.

Röhm and Haas were advised that Glycerosal would be accepted if its superiority over established esters was demonstrated by comparative experiment and unwarranted claims were withdrawn. After waiting in vain for two years for the needed evidence, the Council declared Glycerosal inadmissible to New and Nonofficial Remedies because unwarranted therapeutic claims were made for it (Rule 6) and because it is an unessential modification of established articles (Rule 10).

GRANULAR EFFERVESCENT BROMIDE AND ACETANILID COMPOUND-MULFORD

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Granular Effervescent Bromide and Acetanilid Compound-Mulford has been authorized for publication.

W. A. Puckner, Secretary.

The Council holds that complex mixtures of remedial agents are from every point of view inimical to therapeutic progress and therefore to the public welfare. They are especially objectionable because it is impossible accurately to determine the effects which follow the simultaneous administration of a number of drugs having dissimilar actions, and because the practice of prescribing such mixtures tends to discourage careful consideration of the special needs of the individual patients without which there can be no drug therapy. On the contrary, with the use of such mixtures, therapeutic treatment becomes haphazard and mere guesswork.

The Council, appreciating that long established customs cannot be changed at once, has applied Rule 10, concerning the recognition of mixtures, with the greatest leniency compatible with consistency. When there has been a reasonable doubt concerning the value of a mixture, it has frequently directed that Rule 10 should not apply, pending further clinical trial of such mixture.

In no instance has subsequent experience shown that a strict interpretation of the rule would have worked hardship or injustice. The Council feels that there is no longer warrant for the admission of complex mixtures to New and Nonofficial Remedies, or for the retention of any that have been admitted, unless definite evidence of the therapeutic value of such combinations is available. In accordance with

this decision, several mixtures now described in New and Nonofficial Remedies will be omitted at the expiration of the three year period for which articles are accepted.

Granular Effervescent Bromide and Acetanilid Compound-Mulford is listed in the Appendix to New and Nonofficial Remedies. Each 100 Gm. of the mixture contains sodium bromide, 5 Gm., and acetanilid, 1.5 Gm. According to the label, an amount containing acetanilid, 6.5 grains, and sodium bromide, 22 grains, is to be taken at a dose, to be repeated in half an hour if necessary. For "children," half this dose is advised.

The Council has considered the available evidence for mixtures of this sort, and has reached the conclusion that they are inimical to rational medicine and the public, and therefore in conflict with Rule 10. It holds that the use of mixtures of acetanilid and sodium bromide in fixed proportion is irrational and prone to induce their indiscriminate use by the public. Despite the perfectly frank declaration of the composition of this mixture that is made by the Mulford Company, the "directions" will be followed blindly and the preparation will be given to "children" and "repeated in half an hour, if necessary" in cases in which it would be held unwarranted to administer a dose of 3 grains of acetanilid to a child.

The period of acceptance having expired for Granular Effervescent Bromide and Acetanilid Compound-Mulford, the Council directed its omission from New and Nonofficial Remedies for conflict with Rule 10.

HOLADIN AND BILE SALT MIXTURES

Holadin and Bile Salts-Fairchild; Capsules of Bile Salts, Succinate of Soda and Phenolphthalein-Fairchild; Capsules of Holadin, Bile Salts and Phenolphthalein-Fairchild; Capsules of Holadin, Succinate of Soda and Bile Salts-Fairchild.

Report of the Council on Pharmacy and Chemistry

To explain the omission from New and Nonofficial Remedies of certain mixtures, the Council has authorized publication of the matter which appears below.

W. A. Puckner, Secretary.

The Council holds that complex mixtures of remedial agents are from every point of view inimical to therapeutic progress and therefore to the public welfare. They are especially objectionable because it is impossible accurately to determine the effects which follow the simultaneous administration of a number of drugs having dissimilar actions.

and because the practice of prescribing such mixtures tends to discourage careful consideration of the special needs of individual patients without which there can be no rational drug therapy. On the contrary, with the use of such mixtures, therapeutic treatment becomes haphazard and mere guesswork.

The Council, appreciating that long established customs cannot be changed at once, has applied Rule 10 concerning the recognition of mixtures with the greatest leniency compatible with consistency. When there has been a reasonable doubt concerning the value of a mixture it has frequently directed that Rule 10 should not apply, pending further clinical trial of such mixture.

In no instance has subsequent experience shown that a strict interpretation of the rule would have worked hardship or injustice. The Council feels that there is no longer any warrant for the admission of complex mixtures to New and Nonofficial Remedies or for the retention of any that have been admitted unless definite evidence of the therapeutic value of such combinations is available. In accordance with this decision, several mixtures now described in New and Nonofficial Remedies will be omitted as soon as the three year period for which articles are accepted has expired.

The following preparations are included in New and Nonofficial Remedies, 1918:

Holadin and Bile Salts-Fairchild.—A mixture of holadin, 5 parts, with bile salts-Fairchild, 1 part, put up in 3 grain capsules.

Capsules of Bile Salts, Succinate of Soda and Phenolphthalein.—Each capsule contains bile salts-Fairchild, 0.065 Gm. (1 grain); sodium succinate exsiccated, 0.2 Gm. (3 grains), and phenolphthalein, 0.03 Gm. (½ grain).

Capsules of Holadin, Bile Salts and Phenolphthalein.—Each capsule contains holadin, 0.13 Gm. (2 grains); bile salts-Fairchild, 0.03 Gm. (½ grain), and phenolphthalein, 0.065 Gm. (1 grain).

Capsules of Holadin, Succinate of Soda and Bile Salts.—Each capsule contains holadin, 0.20 Gm. (3 grains); sodium succinate exsiccated, 0.20 Gm. (3 grains), and bile salts-Fairchild, 0.03 Gm. (½ grain).

Oxbile has long been credited with a cholagogue action, which, however, has probably been greatly overestimated. When pure bile salts were placed on the market some years ago, they and their compounds were admitted to N. N. R.

Holadin is said to represent all the constituents of the pancreas and to possess great potency in respect to the sev-

eral enzymes, trypsin, amylopsin, lipase, and the milk-curdling ferment.

It is not clear when such a substance is indicated therapeutically. While it may be useful when there is a deficiency of pancreatin and gastric secretion, it should be used alone.

It is also quite possible that bile salts may have a distinct, though limited, field of usefulness when there is a deficiency of biliary secretion; but the bile salts are best administered alone, or in combination with such laxatives as may be deemed necessary by the physician while keeping in mind the fact that different patients show the widest difference in their reaction to laxatives, making combinations of these agents in fixed proportion irrational.

Phenolphthalein was popularized by nostrum makers; and while it has some therapeutic value, this has been greatly overestimated, and it should be used only in amounts deemed necessary for each patient, preferably alone.

Succinate of sodium was introduced as a saline cathartic, with the claim that it exerts an antiseptic action on the biliary passages and gallbladder. There is no satisfactory evidence to substantiate this claim.

The Council maintains a liberal attitude toward new preparations, but it feels that it is impossible to determine the value of the several constituents of such complex mixtures when used as such; it holds that these mixtures are superfluous and that the several substances of which they are composed should be used singly or at most with greater attention to the individual requirements of the patient than is possible when these fixed mixtures are prescribed.

Despite the fact that these mixtures have been in use for more than nine years, there is no satisfactory evidence that they possess any advantage over the simple laxatives or the preparations of bile or pancreatic extract. They are therefore held to be in conflict with Rule 10, and the Council has directed that they be not included in N. N. R. after Dec. 31, 1918.

Having adopted the preceding report, the Council, in accordance with its regular procedure, submitted this to Fairchild Bros. and Foster for comment.

The following reply was received:

We are entirely at variance with you in the arbitrary conclusion expressed concerning the inimical influence of mixtures on therapeutic progress, the practice of medicine and the public welfare.

If the combinations of Holadin and Bile Salts, etc., in capsules, were ever properly within the scope of New and Nonofficial Remedies, they should be retained. If, however, complex mixtures are to be held as, a priori, unworthy of consideration, the rejection of all would naturally be a logical proceeding.

We believe that the particular combination of Holadin and Bile Salts, etc., have been clearly in the line of therapeutic progress—a natural evolution, improvement and development.

For many years combinations of pancreatic extract and ox gall had naturally suggested themselves.

When we realized the fact that the bile salts were quite clearly the active principles of the bile, and that they must necessarily exist in greatly varying percentages in the official inspissated ox gall, and also because these ox gall products of pharmacy were of extremely varying density, even from that of treacle to resin—and of other objectionable character, we undertook to prepare bile salts.

These combinations are now further justified in view of physiological considerations, the simultaneous secretion of the pancreas and bile, and the state of our knowledge of the function of bile salts, and as co-ferments, promoting and supplementing the pancreas enzymes.

The question suggested as to whether the cholagogic action of ox gall (and bile salts) has been overestimated seems to us no clear purport. The bile salts are obviously employed as the means of administering and thus realizing whatever properties this secretion may have in medicine, of which the cholagogic action is by no means the only consideration.

As for phenolphthalein, which is credited with purely laxative properties, we are at a loss to see any bearing in the remark that phenolphthalein was popularized by nostrum makers. We cannot see that the physician's or chemist's estimate of phenolphthalein, its properties and uses, can be in the least degree influenced one way or the other by the statement that "phenolphthalein has been popularized by nostrum makers."

The phenolphthalein and succinate of soda combinations were originallly both prescribed, and we have simply placed them at the service of the physician without other exploitation of them than that designed to call attention to their use in the conditions indicated.

These combinations are offered in a form which may be administered by the mouth with the best promise of introducing the substance more directly in the intestinal tract during the digestion period, or at such interval after, or prior to, the digestion period, as would best, in the judgment of the physician, meet the indications.

These particular combinations are especially desirable in these "fixed forms" since they are stable and reliable resources at the command of the physicians, the enzymes retaining their stability and potency without material deterioration for many years, and they naturally possess the advantages which are obviously due to the character of the particular pancreas and bile products used in the combinations.

Furthermore, the hygroscopic and soluble organic substances in admixture cannot extemporaneously be so prepared in sealed capsules as to be readily available under the practical requirements of prescribing and dispensing. And we do not believe that those who practice medicine will be in accord with your view that the pancreas substance should necessarily be administered alone, or the bile substance alone.

It now appears that these combinations are to be dropped from New and Nonofficial Remedies in consequence of the view, so stated, that in clinical experience "for more than nine years there is no satisfactory evidence that they possess any advantage over the simple laxatives or preparations of bile or pancreatic extract."

In reply to this we would simply make the following comment:

During these "nine years" these combinations have inevitably been put to an informing clinical trial, because of the fact that they have been employed with success in disorders of the pancreas and bile functions and often in chronic and serious cases where the clinical conditions were obvious and unmistakable.

The reports of these cases come to us from physicians widely separated and each of his own independent initiative. It would seem gratuitous, to say the least, to state that the observers are "disinterested," since it is quite clear that there is no other interest than that of the practitioner and his patient.

It is not a case of a new drug or combinations of new remedies, but simply resources which, upon well grounded reasons, both from a

theoretical and material standpoint, justify clinical trial, and with results which would seem from any ordinary human standpoint to be satisfactory clinical evidence.

As to the interpretation of competent clinical evidence by the Council, we would, in view of the circumstances and without comment, ask to embody in this text this rule:

> "Clinical Evidence."—"To be acceptable, the clinical evidence must offer objective data with such citation of authority as will enable the Council to confirm the facts and establish the scientific value of the conclusions drawn. Clinical data are worthless when the author is not cited. The facts on which claims with regard to the value of a remedy are based must have been rendered accessible for investigation and confirmation by disinterested observers, either through publication or through the records of a hospital or other institution."

To discredit these combinations would seem to us not only unjustified, but sterile of any real advancement in medicine, or of anything in the way of helpfulness to the patient in the class of cases in which these products have been resorted to with benefit; this on no other ground really than the opinion "that they have no advantage over the simple preparations themselves."

Naturally we shall continue to prepare these products and shall continue to take such action as we deem best to bring them to the attention of the physician, for the conduct of our business must remain in the hands of those who are personally responsible for it.

And it is now forty years since we took up this line of work and with the declared intention of devoting ourselves to the applied science of the digestive ferments and "to their development and practical application in every useful purpose in medicine."

We have been consistently in sympathy with the fundamental purpose of the Council, which must first rest upon fact as to the character of the products offered as medicinal agents. The weight of evidence justifies the position that these particular products rationally should be, and as a matter of fact are, of important, special service in the utilization of these organic secretions in medicine.

As explained in the preceding report, the Council holds that complex mixtures of remedial agents are from every point of view inimical to therapeutic progress and therefore to the public welfare. They are especially objectionable because it is impossible to determine accurately the effects which follow the simultaneous administration of a number of drugs having dissimilar actions, and because such a practice tends strongly to discourage careful consideration of the special needs of individual patients without which there can be no therapeutic progress. On the contrary, with their use, therapeutic treatment becomes haphazard and mere guesswork.

The dismissal of the holadin and bile salts mixtures does not involve the question of the usefulness of holadin or of bile salts alone: on the contrary, the possible usefulness of these preparations is admitted in the report. It is the combination of holadin, bile salts, sodium succinate and phenolphthalein to which objection is made.

The statement of Fairchild Bros. and Foster that "these combinations are now further justified in view of physio-

logical considerations" is somewhat misleading. It is true that bile and the pancreatic secretion cooperate in intestinal digestion, but there is no evidence that in every case in which there is a deficiency of one of these secretions there is also a deficiency of the other, and it is an axiom of scientific therapeutics that no drug or remedial agent should be administered except to fill a definite want. Otherwise the practice of therapeutics becomes mere empiricism.

The properties of phenolphthalein are not in the least influenced by the manner of its introduction, as Messrs. Fairchild Bros. and Foster emphasize; but the important fact in this connection is that the popular conception of their actions is greatly influenced by the mode of introduction, and phenolphthalein has been widely advertised in a variety of conditions, so that the popular notion concerning it is not that of scientific therapeutics.

In short, the entire argument of Messrs. Fairchild Bros. and Foster concerning the exploitation of these preparations may be summed up by saying that they have been used by clinicians who believe that good results have followed their use, and that the firm will therefore continue to supply the demand. The tendency of some to use anything brought to their notice, and the readiness of manufacturers to market anything that physicians will use, presents the greatest obstacle to therapeutic progress. There was never a nostrum so irrational or worthless that honest but undiscriminating clinicians could not be found who reported wonderful results from its use.

According to Fairchild Bros. and Foster, these holadin and bile salts mixtures have been in use for some nine years. Yet the Council is not aware of any investigation of their merits that meets the requirements of scientific research.

The Council is not acquainted with a single clinical investigation of their action under conditions which afford satisfactory evidence of their therapeutic value.

It is obviously wholly insufficient for a clinician to report that the use of a mixture was followed by good results. The fallacy of such arguments was demonstrated long ago. He must make a comparison of the results obtained with the remedial agent with those obtained in as nearly similar conditions as possible except for the use of the agent. We are not aware that any such study of the mixtures in question has been made. It is in the last degree irrational to hold that because bile salts are the active constituents of bile, therefore such complex mixtures as these are necessary.

LEDERLE'S POLLEN ANTIGEN

Report of the Council on Pharmacy and Chemistry

The report which appears below was submitted by the referee of the Council in charge of pollen protein preparations to his consultants along with the matter submitted by the Lederle Antitoxin Laboratories in reply for the firm's "own extensive statistics." These investigators endorsed the report; after this the referee submitted it to the Council for action. The Council adopted the report and authorized its publication. W. A. PUCKNER, Secretary.

In 1917, Lederle's Pollen "Vaccine," said to be a pollen extract made from a mixture of "equal parts by weight of the pollens of timothy, red top, June grass, orchard grass, sorrel dock, daisy, maize, ragweed and goldenrod," representing both spring and fall pollens, was declared inadmissible to New and Nonofficial Remedies because (1) the name "vaccine" was incorrectly applied to this plant extract, and (2) because there was no evidence that the pollen mixture represented by the preparation was rational.

Early in 1918, the Lederle Antitoxin Laboratories wrote:

"In deference to the wishes of the Council on Pharmacy and Chemistry in the interests of correct nomenclature, we have decided to change the name of our product heretofore known as Pollen Vaccine, and in future it will be known as Pollen-Antigen.

"In view of this change, we will ask that you reconsider our application for admission for this product into 'New and Nonofficial Remedies.'"

With regard to the Council's decision that there was no evidence for the rationality of the combination, the Lederle Antitoxin Laboratories wrote:

"In all of the studies which we have made of the published researches, and in the consultations we have had with men who have made these researches, we do not find that a necessity for separating these pollens has been shown.

"Furthermore, the clinical data which is available on this subject, including our own extensive statistics, clearly do not indicate any necessity for such separation."

An inquiry was sent to several investigators whose study of the question of pollen sensitiveness warrants their expressing an expert opinion.

There was complete accord in the opinion of all these experts that there appeared no warrant for the use of complex pollen preparations representing both spring and fall pollens.

In advising against the recognition of "spring" and "fall" pollen preparations, one investigator wrote:

"Combined extracts of 'spring' and 'fall' pollens are not advisable. While our experience of the past two years has shown that susceptibility to both forms is much larger than is generally supposed . . . the degree of susceptibility to both varies greatly. Exposure to the

grass pollen is usual in the spring and to the ragweeds (Eastern and Southern States) in the fall, so that both extracts are not indicated at the same time. The principal reason for such a combination is to avoid the necessity of making a diagnostic test, which, however, is an essential factor in the success of this method."

The Council has previously explained:

"In consideration of the essentially experimental status of the use of pollen preparations for the prevention and treatment of 'hay-fever,' such products should be as simple as possible. The Council therefore has decided that, in accordance with the principle of Rule 10, pollen protein preparations, prepared from the pollen of two or more different species of plants, shall be accepted only if there is evidence that the given combination is rational."

There being no acceptable evidence for the use of pollen preparations representing the combined pollen of plants blooming in spring and of those maturing in fall, and because of the tendency for the haphazard treatment of pollenosis, the Council decided not to accept Lederle's Pollen Antigen.

LIQUOR SANTAIVA, S. & D., OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Liquor Santaiva, S. & D., has been authorized for publication.

W. A. Puckner, Secretary.

So far the Council has applied Rule 10 concerning the recognition of mixtures with the greatest leniency compatible with consistency. When there has been a reasonable doubt concerning the value of a mixture, it has frequently directed that Rule 10 should not apply, pending further clinical trial of such mixture.

In no instance has subsequent experience shown that a strict interpretation of the rule would have worked hardship or injustice. The Council feels that there is no longer any warrant for the admission of complex mixtures to New and Nonofficial Remedies or for the retention of any that have been admitted, unless definite evidence of the therapeutic value of such combinations is available.

The Council being engaged in the annual revision of New and Nonofficial Remedies, the referee in charge of santal preparations reported that the three year period of acceptance had expired for Liquor Santaiva (Sharp & Dohme).

The referee held that Liquor Santaiva, S. & D., declared to be a solution of santal oil and copaiba with aromatic oils in a mixture of alcohol and water, is plainly in conflict with the current interpretation of Rule 10, because there was no sound evidence to indicate that any useful end is

gained by the simultaneous administration of santal oil and copaiba in any proportion, and that so, of course, there is no evidence of the special advantage in the fixed proportions represented by the mixture. He pointed out that the formula is essentially a survival of the discredited shotgun gonorrhea mixtures and therefore recommended that its acceptance be not continued.

The Council agreed to the recommendation of the referee and directed that Liquor Santaiva, S. & D., be omitted from New and Nonofficial Remedies.

MALTZYME, MALTZYME WITH CASCARA SAGRADA, MALTZYME WITH COD LIVER OIL, MALTZYME FERRATED AND MALTZYME WITH YERBA SANTA OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of the Maltzyme preparations has been authorized for publication.

W. A. Puckner, Secretary.

In 1916, the Council voted to omit Maltzyme with Hypophosphites, and Maltzyme with Phosphate of Iron, Quinine and Strychnine. At that time the labels used on the Maltzyme preparations still in New and Nonofficial Remedies contained a list of Maltzyme combinations which included those which had been dismissed. As the Council does not permit an accepted article to be used as a means of advertising an article not accepted, it voted to continue the following preparations for a period of three years on condition that reference to the deleted articles be omitted from the labels when those then in stock had been used up: Maltzyme, Maltzyme with Cascara Sagrada, Maltzyme with Cod Liver Oil, Maltzyme Ferrated and Maltzyme with Yerba Santa. While the Maltzyme Company made no definite agreement to revise its advertising propaganda in accordance with the Council's requirements, the Maltzyme preparations were retained in the belief that in due time the required revision of the labels would be made.

The Council being engaged in preparing the 1919 edition of New and Nonofficial Remedies, the referee in charge of malt extracts reported that the Maltzyme Company had not revised its labels in accordance with the stipulation of the Council. The referee further reported he had become

convinced that the claim that Maltzyme is "rich in malt enzymes" is unwarranted and that the term "Maltzyme" (malt plus enzyme) is misleading; this because of the recognized instability of malt extracts (Jour. A. M. A., March 30, 1912, p. 954) and because the Maltzyme Company makes no definite statement with regard to the diastase (malt enzyme) content of its preparations.[1] For this reason it had been the referee's intention to propose the deletion of all Maltzyme preparations when their period of acceptance expired in 1919. As, however, the present Maltzyme preparations are in contravention with the Council's requirements, he recommended that the acceptance of these preparations be canceled now.

The Council agreed to the recommendation of the referee and directed that Maltzyme, Maltzyme with Cascara Sagrada, Maltzyme with Cod Liver Oil, Maltzyme Ferrated, and Maltzyme with Yerba Santa be omitted from N. N. R.

METHAFORM OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Methaform has been authorized for publication.

W. A. PUCKNER, Secretary.

Methaform is the proprietary name applied by F. Stearns & Co. to chlorbutanol.

Being engaged in the annual revision of New and Nonofficial Remedies, and the term of acceptance for Methaform having expired, a trade package was purchased to determine if the product was marketed in compliance with the rules of the Council. It was then found that a circular was wrapped with the trade package which advertised Methaform Inhalant, a preparation not accepted for New and Nonofficial Remedies.

For obvious reasons, the Council does not countenance the use of an accepted article as a means of advertising an article not accepted. Accordingly F. Stearns & Co. was advised that the Council would be obliged to withdraw the

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1. Manufacturers are warned by the Department of Agriculture, through the Bureau of Chemistry, that combinations claiming to contain digestive enzymes must be active when sold. If preparations tend to deteriorate in a short time, each lot should be dated and not sold after the period when they become inactive. While every manufacturer must be considered innocent until proved guilty, and ignorant until proved knowing, it is a matter of knowledge that manufacturers have marketed their various digestive mixtures with full appreciation of their worthlessness.—(Jour. A. M. A., Dec. 19, 1914, p. 2234.)

acceptance of Methaform unless the objectionable circular was omitted from the Methaform packages. Stearns & Co. did not give the requested assurance, and therefore the Council directed that Methaform be omitted from New and Nonofficial Remedies.

PINEAL GLAND, RED BONE-MARROW AND THYMUS GLAND AND THEIR PREPARATIONS OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of pineal gland, red bone-marrow and thymus gland and their preparations has been authorized for publication.

W. A. Puckner, Secretary.

Pineal gland, red bone-marrow and thymus gland were admitted to New and Nonofficial Remedies when these products gave promise of having therapeutic value.

The term of acceptance for the preparations of pineal gland, red bone-marrow and thymus gland having expired, the referee in charge of animal organ preparations recommended in his report for the annual revision of N. N. R. that these products and the general articles describing them be omitted from New and Nonofficial Remedies. He held that the experimental and clinical experience with them leads to the conclusion that they are without value.

In accordance with the recommendation of the referee, the Council voted that the following preparations be omitted from New and Nonofficial Remedies: Desiccated Pineal Gland-Armour; Pineal Gland Tablets-Armour; Extract of Red Bone-Marrow-Armour; Desiccated Thymus-Armour; Thymus Tablets-Armour.

As a matter of record, the descriptive articles for pineal gland, red bone-marrow and thymus gland, which appeared in New and Nonofficial Remedies, 1918, are given below.

Pineal Gland

The functions of this gland have not yet been established but there is some pathological and some experimental evidence that there is a relation between the gland and some processes of development and growth; the nature of this relation is unknown. Adiposis is a frequent sign of disturbed pineal function, but observers are not agreed whether to interpret this as indicating hypofunction or hyperfunction, or possibly a concurrent disturbance of the pituitary. In some instances intravenous injections of pineal extract have

seemed to cause a distinct fall in blood pressure. It has been inferred from observations in cases of pineal tumors in the young that the gland in young individuals furnishes a secretion which inhibits growth, particularly the development of the reproductive glands, but the results of experimental administration of pineal substance orally have led other observers to infer that the pineal secretion favors physical and possibly mental and sexual development. It has been suggested that, as all evidence points to the fact that the function of the pineal gland is one of early life, extract of adult pineal glands might be expected to be inert. Experiment has also indicated greater activity in glands obtained from young animals than in those obtained from older ones. The Council has decided to admit preparations of pineal gland to New and Nonofficial Remedies simply for experimental purposes.

Red Bone-Marrow

Red bone-marrow consists largely (more than 90 per cent.) of fat. In new-born animals a third or more of this fat consists of lecithin. The marrow of the bones of new-born animals contains iron (up to 1 per cent. or more) in various forms of organic combination. Both lecithin and iron decrease rapidly in the first weeks after birth. The commercial preparations contain very variable amounts of these constituents.

Actions and Uses.—Red bone-marrow is supposed to stimulate the formation of red blood corpuscles; whatever action it may have in this direction is probably due largely to the iron and lecithin which it contains.

It is said to be useful in simple and pernicious anemias.

Thymus Gland

Little is known as to the functions of the thymus, but it is believed to have an important relation to growth. There also seems to be some relation between the thymus and thyroid, for the former is frequently abnormal in diseases involving the latter (hyperthyroidism).

The use of thymus is purely empirical. It has been employed in the treatment of hyperthyroidism, rickets, tuberculosis, hemophilia, and infantile marasmus and atrophy; its use in the latter conditions is said to be the most promising. It is claimed on very doubtful grounds to exert a somewhat favorable effect in certain cases of cancer.

PIPERAZINE AND LYCETOL OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Piperazine and Lycetol has been authorized for publication.

W. A. Puckner, Secretary.

Piperazine (diethylenediamene) and Lycetol (a methyl derivative of diethylenediamene) were accepted for New and Nonofficial Remedies in 1906. Both Piperazine and Lycetol were asserted to be efficient uric acid solvents and efficacious remedies in the treatment of gout and rheumatism. These products have been retained until now because there was no investigation which definitely showed their uselessness as uric acid solvents, though their use is generally admitted to have been disappointing.

From an exhaustive and critical study of the available evidence, Hanzlik (Jour. Lab. & Clin. Med., February, 1917) concluded that scientific evidence, though limited, and clinical opinion indicate that Piperazine is valueless in gout and that there is sufficient scientific evidence to indicate the worthlessness of Lycetol.

The referee in charge of Piperazine and Lycetol recommended that these products be omitted from New and Nonofficial Remedies for the reason that they have been sufficiently tried to justify the conclusion that they are not of value. The period of acceptance having expired, the Council directed that Piperazine and Piperazine Tablets (The Bayer Company, Inc.) and Lycetol (The Bayer Company, Inc.) be omitted from New and Nonofficial Remedies.

SODIUM OLEATE OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

Sodium oleate was described in New and Nonofficial Remedies because of a demand for an oleate of sodium created by the advertising for certain proprietaries claimed to contain sodium acid oleate. As this so-called sodium acid oleate was of indefinite composition (Jour. A. M. A., Feb. 22, 1908, p. 627), the Council decided to describe sodium oleate.

The description of sodium oleate as it appears in New and Nonofficial Remedies, 1918, is essentially that of the pharmacopœial *Sapo*—in fact, the label for sodium oleate-Merck gives "Soap U. S. P. IX" as a synonym.

Since the official soap meets all requirements, the Council decided to omit sodium oleate and the accepted brand from New and Nonofficial Remedies. It directed that the monograph on sodium oleate which appears below be transferred to the Council Reports as a matter of record.

W. A. Puckner, Secretary.

SODIUM OLEATE. — Sodii Oleas. — $NaC_{18}H_{33}O_{21}$. — The sodium salt of oleic acid.

Actions and Uses.—Sodium oleate is antacid and mildly laxative. It is commonly added to laxative pills. It has been claimed without any definite evidence that it is especially useful in disease of the biliary tract.

Dosage.—From 0.12 to 1.3 Gm. (2 to 20 grains).

NOTE.—This preparation should not be confounded with the preparations sold as "acid sodium oleate" or "sodium oleate, acid," which are mixtures of sodium oleate and free oleic acid, containing from about 5 to 30 per cent. of the latter.

Sodium oleate may be obtained by neutralizing sodium hydroxide with oleic acid.

Sodium oleate is a white solid, which crystallizes from absolute but not from aqueous alcohol. When heated it melts and burns, leaving a residue of sodium carbonate. It is soluble in about 10 parts of water, in about 20 parts of alcohol, and in about 100 parts of boiling ether. When dissolved in water it is partly decomposed (hydrolyzed) into oleic acid and sodium hydroxide; hence its aqueous solution has an alkaline reaction to phenolphthalein; its solution in strong alcohol is neutral to this indicator. It is precipitated from its aqueous solution by saturation with sodium chloride.

From an aqueous solution of sodium oleate, mineral acids separate oleic acid, collects at the surface of the liquid, in an oily layer. If a solution of 5 Gm. of sodium oleate in 50 Cc. of water be mixed with 3 Cc. of tenth-normal oxalic acid solution, the subsequent addition of phenolphthalein test solution should not produce a pink coloration. An aqueous solution of sodium oleate (1:20) should remain unchanged in color upon the addition of ammonium sulphide test solution; and on acidulating another portion of the solution with hydrochloric acid and filtering, the filtrate should remain unchanged in color when an equal volume of hydrogen sulphide test solution is added, and the mixture is allowed to stand well stoppered in a warm place for half an hour (absence of metallic impurities).

STANOLIND LIQUID PARAFFIN OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

As explained in the report which follows, "Stanolind Liquid Paraffin" was omitted from New and Nonofficial Remedies at the request of the proprietors. Announcement of this omission was made in the preface to New and Nonofficial Remedies, 1918, but publication of the Council's report was postponed pending actual conflict with the rules. The Council now authorizes publication of the report because a circular indirectly advertising the product to the public was found enclosed with the trade package of Stanolind Liquid Paraffin.

W. A. PUCKNER, Secretary.

Stanolind Liquid Paraffin was admitted to New and Nonofficial Remedies in 1916, when its method of marketing conformed to the rules of the Council. This brand of liquid petrolatum, by action of the Council, has been omitted from New and Nonofficial Remedies on request of the Standard Oil Company of Indiana, its manufacturer, who wrote to the Secretary of the Council stating that:

"In order that our facilities for the manufacture of this oil shall be constantly engaged, it will be necessary for us to find sales on a larger scale than in the past. To do this under our present advertising and marketing arrangement we feel will be impossible."

This letter, in addition, suggested "that physicians are not prescribing Stanolind Liquid Paraffin in any considerable proportion of their orders" and "that the situation which now confronts us would not be materially helped if Stanolind was specified in all such prescriptions." Further, the Council is asked to consider whether it "might be willing to declare this preparation as not a Council product," on the alleged grounds that "liquid paraffin is not medicinal in its action and passes through the digestive tract in practically unaltered condition."

The Council holds that Stanolind Liquid Paraffin is a drug, and that, therefore, its direct advertising to the public is in contravention of the Council's rules. Constipation should be treated by dietary and hygienic means. Evacuants are only temporary measures. Liquid petrolatum is medicinal; it greatly modifies the intestinal flora; it acts as a lubricant and emollient; it modifies the absorptive powers of the intestinal mucous membrane; it is capable of influencing the digestion of fats. In short, liquid petrolatum, being a drug, its indiscriminate and excessive use should not be encouraged.

TABLETS ACET-PHENETIDIN COMPOUND, P.-M. CO. OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Tablets Acet-Phenetidin Compound, P.-M. Co. has been authorized for publication.

W. A. Puckner, Secretary.

The Council holds that complex mixtures of remedial agents are from every point of view inimical to therapeutic progress and therefore to the public welfare. They are especially objectionable because it is impossible accurately to determine the effects which follow the simultaneous administration of a number of drugs having dissimilar actions, and because the practice of prescribing such mixtures tends to discourage careful consideration of the special needs of individual patients without which there can be no rational drug therapy. On the contrary, with the use of such mixtures therapeutic treatment becomes haphazard and mere guesswork.

The Council, appreciating that long established customs cannot be changed at once, has applied Rule 10, concerning the recognition of mixtures, with the greatest leniency compatible with consistency. When there has been a reasonable doubt concerning the value of a mixture, it has frequently directed that Rule 10 should not apply, pending further clinical trial of such mixture.

In no instance has subsequent experience shown that a strict interpretation of the Rule would have worked hardship or injustice. The Council feels that there is no longer warrant for the admission of complex mixtures to New and Nonofficial Remedies or for the retention of any that have been admitted, unless definite evidence of the therapeutic value of such combinations is available. In accordance with this decision, several mixtures now described in New and Nonofficial Remedies will be omitted at the expiration of the three year period for which articles are accepted.

Tablets Acet-Phenetidin Compound, P.-M. Co. (The Pitman-Moore Co., Indianapolis, Ind.) are listed in the Appendix to New and Nonofficial Remedies. Each tablet contains acetphenetidin, 0.23 Gm. (3½ grains); caffein, 0.016 Gm. (¼ grain), and sodium bicarbonate, 0.08 Gm. (1¼ grain). The Council has considered the evidence submitted to establish the value of this combination, and has reached the conclusion that the product is in conflict with Rule 10. Accordingly, it has directed that the preparation be omitted from New and Nonofficial Remedies at the expiration of the three year period of acceptance (Dec. 31, 1918).

It is generally admitted that mixtures of acetphenetidin and caffein or acetanilid and caffein may be more effective in certain cases than either drug alone in relieving headaches. Acetphenetidin, acetanilid and caffein are active drugs, and their doses should be regulated with especial reference to the tolerance of the patient. Acetanilid and acetphenetidin should be given in the smallest effective doses, preferably using very small initial doses and repeating as may be necessary. It is irrational to administer in fixed proportions such drugs as caffein and either acetanilid or acetphenetidin, because their rates of elimination are not at all the same, and their initial doses vary with different patients. What has been said about the doses of acetphenetidin and caffein applies equally to sodium bicarbonate. The gastric acidity of individuals varies so widely that any antacid should be administered alone, and in doses and intervals required to secure the desired effect.

Fixed formula mixtures containing acetphenetidin or acetanilid have led to self-medication to an alarming degree and even to drug addiction. The physician should give his patient careful attention to the individual needs of the condition and to avoid such ready-made mixtures.

WESTERFIELD'S DIGITALIS TABLETS

Report of the Council on Pharmacy and Chemistry

The Council has adopted the following report and authorized its publication.

W. A. Puckner, Secretary.

Westerfield's Digitalis Tablets (The Westerfield Pharmacal Co., Dayton, Ohio) are claimed to represent a fat free tincture of digitalis and to be "enteric coated." It is claimed that because of this coating these tablets pass the stomach unchanged and dissolve in the intestine, and that this obviates any possibility of gastric disturbance.

The circular which sets forth the asserted advantages of the tablets states that digitalis contains a fat which is an irritant to the gastric membrane. It also contains the following:

"We feel no hesitation in saying that if this remedy is given a fair trial where it is properly indicated, the result obtained will be a gratifying surprise.

"It is a common expression from physicians who have tried this remedy to say, 'Surely I have never used Digitalis before.' "

If these quotations mean anything, they imply that these tablets present a distinct advance in digitalis therapy. There is no warrant for such a claim. The statement with reference to the occurrence of an oil in digitalis is partly false and partly misleading. Tincture of digitalis, which the tablets are claimed to represent, is fat free; the fixed oil that is present in the drug is not soluble in 70 per cent. alcohol, the menstruum used for the preparation of the official tincture of digitalis. Furthermore, a fairly large amount of this oil (such as is present in 100 therapeutic doses of the drug) is incapable of causing gastric disturbance. Gastric disturbance is a side action that is inseparable from slight overdosage with all true digitalis bodies and is not in any way due to local gastric action. The claim that such action is prevented by the use of enteric pills or tablets is obviously false and misleading.

The alleged "common expression from physicians who have tried this remedy" does not constitute acceptable evidence of the value of the preparation.

The Council declared Westerfield's Digitalis Tablets inadmissible to New and Nonofficial Remedies because unwarranted therapeutic claims are made for this product.

When the preceding report was submitted to the Westerfield Pharmacal Co., a reply was received indicating that the firm did not know that progressive manufacturers had discontinued the claim that "fat free" digitalis preparations were devoid of gastric effects. It also submitted a revised circular, which, however, reiterated the claim that the tablet presented a distinct advance in digitalis therapy in that it was "fat free," and coated to prevent disintegration in the stomach.

Since tincture of digitalis and extract of digitalis are practically devoid of fatty material, and since it is now well known that the fat does not cause gastric disturbance and that therapeutic doses of digitalis do not exert a local irritant action on the stomach, the manufacturer's product and the claims made for it merely tend to perpetuate old errors.

The Council declared Westerfield's Digitalis Tablets inadmissible to New and Nonofficial Remedies on the ground that this presents an unessential modification of pills of an official substance. It directed publication of its report with this explanation.

XEROFORM-HEYDEN AND BISMUTH TRIBROMPHENATE-MERCK OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report on Bismuth Tribromphenate-Merck and Xeroform-Heyden. These two products were found not to comply with the standards for bismuth tribromphenate adopted for New and Nonofficial Remedies, and hence could not be retained. As the manufacturers of both products announce that efforts toward the production of a satisfactory product are continued, the omission of the two brands is without prejudice to their reacceptance when a satisfactory product becomes available.

W. A. Puckner, Secretary.

The referee in charge of bismuth preparations submitted the following report of the A. M. A. Chemical Laboratory which shows that Xeroform-Heyden and Bismuth Tribromphenate-Merck do not comply with the adopted standards for bismuth tribromphenate.

Some time ago a request was received from the Medical Section of the National Council of Defense for a report

on a brand of bismuth tribromphenate. In accordance with this request the firm's product was examined, and at the same time and for comparison, an examination was also made of a specimen of bismuth tribromphenate received from Merck and Company, October, 1915, and of another specimen of bismuth tribromphenate "Xeroform-Heyden" obtained from the Chicago branch of the Heyden Chemical Works in April, 1918.

The examination brought out that the bismuth tribromphenate submitted to the national Council of Defense contained a large amount of uncombined tribromphenol, while the specimen of Xeroform-Heyden contained an excessive quantity of bismuth.

When the latter finding was submitted to the Heyden Chemical Works, the firm stated: "The product had to be made in this country after importations from Europe became impossible and the first lots were not fully up to the standard . . ." The firm stated that it could now furnish a product which it considered fully equal to that which was previously imported, and offered to submit "samples of the new material."

Having been requested to do so, a specimen of Xeroform-Heyden was received from the Heyden Chemical Works, New York. This and a second specimen, purchased from a Chicago wholesale drug house, were examined. Whereas the standards for bismuth tribromphenate which had been formulated by the Laboratory and accepted by the Heyden Chemical Works required that the product should contain from 40 to 49 per cent. of bismuth and contain not more than 3.3 per cent. of uncombined tribromphenol, the specimen purchased in Chicago contained 67.7 per cent. of bismuth, while the specimen received direct from the Heyden Chemical Works contained 24 per cent. of uncombined tribromphenol. When this result was reported to the Heyden Chemical Works, the firm replied:

"It seems that we are not yet in a position to supply a product that answers a uniform standard and that we have to continue our efforts in this direction.

"We will take this matter up with you again as soon as we have been successful . . ."

At the time when the preceding examination was being made, bismuth tribromphenate-Merck could not be obtained from the Chicago wholesale houses. A request sent to Merck and Company for a specimen of the market supply brought the information that the product was temporarily unavailable. Though unable to supply the product, the firm gave valuable advice for a revision of the somewhat loosely drawn tests for bismuth tribromphenate in New and Nonofficial Remedies, 1918.

Recently (November, 1918) Merck and Company sent a specimen of its product labeled "Bismuth Tribromphenate-

Merck" "Merck and Company, New York, Distributors and Guarantors," and wrote ". . . You will notice this sample conforms in nearly all details to the tests we submitted with our letter of June 4th. We have been able to produce better goods, but just at present unsatisfactory starting material confronts us. The sample conforms to N. N. R., 1918, but will not meet the test for uncombined tribromphenol submitted by you in your letter of September 4th . . ."

Examination of the specimen demonstrated that it was soluble to a considerable extent in alcohol (the N. N. R., 1918, description provides that it should be only slightly soluble in alcohol) and according to the standards adopted for New and Nonofficial Remedies, 1919, contains 18 per cent. uncombined tribromphenol (more than five times the permitted amount).

In view of the Laboratory's report, the referee recommended that the acceptance of Xeroform-Heyden and Bismuth Tribromphenate-Merck be withdrawn, without prejudice to their reinstatement when satisfactory products are again offered for sale. The Council adopted the recommendation of the referee, and accordingly Xeroform-Heyden and Bismuth Tribromphenate-Merck are omitted from New and Nonofficial Remedies, 1919.

When the Laboratory's findings with regard to Xeroform-Heyden and the action of the Council deleting the article from New and Nonofficial Remedies was reported to the Heyden Chemical Works, the firm expressed regret that efforts to produce a product equal to that formerly obtained from Germany had so far not been successful and announced that it had decided to withdraw Xeroform-Heyden from the market for the present.

When Merck and Company was advised in regard to the report of the Laboratory and the Council's action, this firm questioned the feasibility of producing a product meeting the Council's standards and suggested that the test for free tribromphenol be revised to permit as much as 15 per cent. of this constituent. When Merck and Company was reminded that its product, submitted in 1915, essentially complied with the adopted standards and that the estimate of the therapeutic value of bismuth tribromphenate is based on a product essentially free from alcohol-soluble material, the firm replied:

"As stated in our letter of the 12th inst. we do not wish to market the chemical unless it meets all legitimate requirements of the physicians that use it. If, therefore, your standard proves to be good and it is commercially possible to make supplies conforming to it, we shall do so. We shall discontinue the article unless it is of suitable quality."

LAY MEDICINES

The preparations discussed under this head are intended primarily for sale to the general public. Their examination by the Council was requested because the proprietors, having proposed their use by the medical department of the U. S. Army, were informed by the Surgeon General's Office that proprietary and unofficial remedies would not be considered for use in the Army until after they had been examined by the Council on Pharmacy and Chemistry.

CREAM OF MUSTARD REFUSED RECOGNITION

Report of the Council on Pharmacy and Chemistry

Cream of Mustard, The Cream of Mustard Co., South Norwalk, Conn., is said to be made by mixing 2 drachms of oil of mustard and 2 drachms of oil of turpentine with one pound of white petrolatum. According to the label it is "for Tonsillits, Rheumatism, Sore Muscles, Croup, Pleurisy, Frosted Feet, Sore Throat, Neuralgia, Sprains, Bronchitis, Headache, Chilblains, Stiff Neck, Congestion, Bruises, Asthma, Lumbago, Pains and Aches, Colds in Chest."

The Council refused recognition to Cream of Mustard:

Because it is a simple pharmaceutical mixture of well-known ingredients and has no advantage over established rubefacients which every physician knows how to prescribe and every pharmacist to compound. Incidentally, the name "Cream of Mustard" is misleading and not descriptive of the composition of this pharmaceutical mixture of oils of mustard and turpentine.

GERMASEPTIC LUBRICANT (BING)

Report of the Council on Pharmacy and Chemistry

Germaseptic Lubricant (Bing) is stated by its owner, Charles M. Griswold, St. Petersburg, Fla., to have the following composition: Mercury Salicylate, 2 per cent.; Quinine Salicylate, 1 per cent.; Methyl Salicylate, Q. S. to saturate; Zinc Oxide, 2 per cent.; Thymol, Eucalyptol, Menthol, AA Q. S. to saturate; Boric Acid, 6 per cent.; F. E. Delphinnium, 5 per cent.; Pino Cresol equal to Carbolic Acid, Pleasant odor and soluble, 2 per cent.; Alcohol, 6 per cent.; Glycerine, 12 per cent.; Normal Saline Lubricant Bass Q. S., 100 per cent.

Pino Cresol is said to be "Liq. Cresolis Comp. combined with Oil Pine Needles as deodorant."

Germaseptic Lubricant (Bing) is marketed in small collapsible tubes (one tube was found to contain 6 Gm.), said

to be sufficient for "25 to 30 applications." It is said to be "a handy little tube which you can carry in your waistcoat pocket."

According to the label, Germaseptic Lubricant (Bing) is a "Safe and Sure Germ Destroyer for Pimples, Cold Sores, Fever Blisters, Boils and Skin Irritations. Absolutely Prevents Venereal Diseases." According to the information submitted to the Council, the preparation is said to be indicated for the "Prevention of Gonorrhea, Syphilis, Tetanus, and all bacterial diseases within its germicidal report" and for "eradicating body lice."

The Council declared Germaseptic Lubricant (Bing) inadmissible to New and Nonofficial Remedies because it is an irrational, complex, indefinite, and semisecret mixture for which unwarranted and dangerous claims are made without declaration on the label of the poisonous mercury compound and under a name which is not descriptive of its composition.

In detail, the preparation is in conflict with the rules of the Council:

Rule 1.—In the asserted formula the amounts of some of the potent ingredients in a given quantity of the preparation are not given, and the identity of the substances which constitute the "normal saline lubricant base" is not declared.

Rule 4.—The recommendation on the label to use the preparation for "Pimples, Cold Sores, Fever Blisters, Boils and Skin Irritations" is likely to lead the public to depend on it in conditions that are serious and which, in the interest of the patient and the public, should receive intelligent treatment.

Rule 6.—The assertion that it "Absolutely Prevents Venereal Diseases" is a gross and wanton exaggeration, particularly when considered in connection with the claim that the contents of one tube are sufficient for 25 to 30 applications. It would be positively dangerous to assume that a semisolid mass containing only 2 per cent. of mercury salt can be relied on as a prophylactic against venereal infection.

Rule 7.—The label does not give warning that this preparation (advised for "cold-sores") contains the potent and poisonous mercuric salicylate.

Rule 8.—The name does not indicate the potent ingredients of this pharmaceutical mixture.

Rule 10.—The combination in one mixture of a mercury compound, quinin salt, zinc oxid, delphinium (stavesacre) and cresol (even if the remaining ingredients are considered as vehicles or "flavors") is irrational.

NAZOL

Report of the Council on Pharmacy and Chemistry

Nazol (Nazol Antiseptic Co., Galveston, Texas) is marketed in the form of small vials containing a strip of cotton to each of which, it is said, there has been added "4 drops each, of menthol, phenol, creosote, camphor, turpentine and eucalyptol." For use, a small piece of Nazol is placed in each nostril, and according to the label is "for continuous inhalations" and is asserted to be "remedial in respiratory diseases and protective against infection." According to the circular wrapped with Nazol, it is:

"Remedial in Colds, Coughs, Catarrhs, Incipient Consumption and LaGrippe. Protective against all above mentioned, and against Measles, Mumps, Whooping Cough, Scarlet Fever, Diphtheria, Meningitis, Infantile Paralysis and other diseases acquired by respiration."‡

There is not a shred of evidence that the inhalation of minute quantities of the heterogeneous mixture of drugs said to be contained in Nazol has any power to prevent or to influence favorably the conditions for which its manufacturer recommends it. The use of Nazol is bound to give its user a false sense of protection from infectious diseases and thus lead to a neglect of proper hygienic and curative measures against disease. Nazol is the noninforming name of an irrational combination of drugs, sold under unwarranted, misleading and false claims.

O'GRADY'S MEDICATED MINERAL CREAM OF SULPHUR

Report of the Council on Pharmacy and Chemistry

The manufacturer of O'Grady's Medicated Mineral Cream of Sulphur furnishes no information with regard to the composition of his preparation, except the ambiguous statement that it is "A Mineral Compound Liquid Sulphur."

The label contains directions for the use of this preparation for "cuts, wounds, ulcers, old sores, all skin breaks," etc. The label also includes the recommendation "For Treatment of Inflammatory Rheumatism, Erysipelas, White Swelling, Goiter, Bronchitis, Lung Fever, Pleurisy, Pains in the Body and Limbs, Inflammation of the Bowels, Kidneys and Bladder, Chilblains, Corns, Bunions and Callouses." It bears

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‡When the Council's report was sent to the Nazol Antiseptic Co. for comment, the following statement was made with regard to the recommendations for the use of Nazol:

"NAZOL is not heralded as a cure, nor as a protective against any disease to the exclusion of other remedies, but as the simplest method known, as an auxiliary to other means, in dealing with respiratory diseases."

the claim that the preparation banishes "Blood Poison of every description," and that by its use goiter is "removed in a short time."

The A. M. A. Chemical Laboratory reports that, though no exhaustive examination of the preparation has been made, it evidently is essentially the familiar calcium polysulphide solution which had its vogue many years ago. It was first introduced as Vleminckx' solution and has since been disguised under various names: "sulphurine," "golden lotion," "yellow lotion," "liquid sulphur," "soluble sulphur," "sulphume," "sulphurro," etc.

O'Grady's Medicated Mineral Cream of Sulphur is a secret remedy marketed under a nondescriptive name and with claims which are unwarranted, misleading and dangerous.

WORLDS WONDER REMEDY

Report of the Council on Pharmacy and Chemistry

Worlds Wonder Remedy is said to be prepared by macerating "the leaves of certain cactus plants, among them being the 'Alligator Tail Cactus,' the 'Philo' cactus and several other species of cactus" in brandy. No evidence is submitted in regard to the possible properties of the "Alligator Tail," the "Philo" cactus or the identity and properties of the "other species." Neither are the quantities of the leaves in a given amount of the wonder remedy declared. It is claimed "We have also found this medicine to be a very good cure for nervousness, headache and all pains of the body, especially stomach trouble, indigestion, cancer of the stomach and we have also given it to people sick at this time of the year and they did not know what ailed them but it made them feel fine."

The Council has no evidence that this preparation has therapeutic virtues, and in the absence of such proof declares the claims unwarranted and preposterous.

YOUNG'S PLURASAV NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

"Young's Plurasav," according to a cursory examination made in the A. M. A. Chemical Laboratory, is a camphor cerate which, according to the label, "contains 1.875 grains opium to each ounce."

When requesting consideration of his preparation, Mr. W. H. Young (The Plurasav Co., Columbus, Ga.) submitted a

"list of ingredients" composing the product. When the Council's conclusions with regard to his preparation were submitted to Mr. Young, he objected to publication of the "list of ingredients."

"I have no objection at all to your publishing the fact that you consider it a menace to the public health, but I do object to your betraying my confidence in publishing in your Journal or anywhere else the ingredients. Without making any idle threats, I will say that if you undertake to do this, that you lay yourselves liable to a suit for damages."

The Council gladly conforms to the proprietor's desire to preserve the secrecy of his formula, for the "list of ingredients" contained but five items, while an advertising circular gives "directions for using Young's Plurasav a scientific combination of six efficient curative remedies . . ." and thus one gives the lie to the other.

The label for Young's Plurasav contains the following:

"External treatment of Pneumonia, Pleurisy and all congestion and inflammations of Lungs, Chest and Throat, and Rising Breast in nursing mothers, spread on cotton cloth and cover well lungs and chest or throat as indicated."

The Plurasav carton advises "Plurasav" for the treatment of:

"All Congestions and Inflammations of the Lungs and Chest, Pneumonia, Pleurisy, Bronchitis, Whooping Cough, Sore Throat, Asthma, LaGrippe, Croup, Chest Colds, Hoarseness, Rising Breast, Etc."

"Plurasav" is an irrational mixture—a survival of the days of camphor and goose grease embrocations. The implied advice in the advertising circular to depend on this mixture as a curative agent in the treatment of serious conditions is a menace to the public health.

INDEX OF PROPRIETARIES, MANUFACTURERS AND AGENTS