disease. Since then Strumpell⁷ has reported a similar case, drawing attention to the similarity or relationship of these two curious clinical pictures. Westphal⁸ himself has reported a case of pseudosclerosis with necropsy findings. He was able to discover distinct changes in the nervous system, chiefly of the glia nuclei, and more especially in the gray substance of the large ganglia of the cerebrum, and also in the dentate nucleus of the cerebellum. The nuclei of the ganglia-cells were enlarged, altered in shape, and were deficient in chromatin substance. In addition, the liver was distinctly reduced in size and presented a cirrhotic appearance. In reporting this case Westphal calls particular attention to the relationship that pseudosclerosis seems to bear to this peculiar morbid process, characterized by pigmentation of the skin, cirrhosis of the liver, tremors and mental and nervous phenomena. It is my belief that the first case here recorded might belong to this group.

1710 Locust Street.

THE PRESENT STATUS OF ORGANIC IODIN PREPARATIONS *

FRANKLIN C. MCLEAN, M.S., M.D.

PORTLAND, ORE.

The flood of organic preparations of the various metals introduced into therapeutics during the past few years has carried with it a considerable number of organic preparations of the non-metallic elements, chiefly the iodids and bromids. The advantages of these preparations over the older inorganic combinations have in general not been carefully considered by the makers or users, but the popularity earned by the organic preparations of arsenic and mercury has led manufacturers to seek new fields of endeavor. In a previous communication¹ I reviewed the evidence regarding the various organic iodine preparations on the market. Since that time some new evidence has been brought forward, and a summary of our knowledge at the present time seems desirable.

The larger number of commercial preparations resolve themselves naturally into two classes: (1) iodine products of the higher fats or fatty acids and (2) iodized albumins. These two classes are so dissimilar that they must be considered separately.

The chief iodized fats and fatty acids on the market at the present time are Iodipin (Merck), Sajodin (Farbenfabriken von Elberfeld), and Iodival (Knoll & Co.) These substances are products of the addition of iodine to the higher fats or fatty acids or their derivatives, and contain varying amounts of iodine. They are sufficiently similar in their characteristics to allow of their being considered together. The advantages over the alkaline iodids claimed by the manufacturers are chiefly as follows: (1) absence of gastro-intestinal irritation, (2) slower absorption, (3) longer retention in the body and a more uniform rate of excretion, and (4) less tendency to produce iodism. The first claim is in general well substantiated, as all of these sub-

stances are bland and unirritating, the iodine being so firmly bound in the molecule as to be inactive locally. These substances are in general absorbed without much change in their composition, the absorption being similar to that of fatty acids, and much slower than that of the alkaline iodids. While 75 per cent. of the iodine given in the form of potassium iodide is excreted in the urine within twelve hours, and the highest amount in the urine is in the second hour, the absorption and elimination of the iodized fats is much slower. When Sajodin is given, iodine does not appear in the urine until after from one to three hours, and while the highest point in the excretion is reached within twelve hours the amount excreted remains high for thirty-six hours, giving a much more uniform rate of excretion. Following absorption, as shown by me,² the iodized fats are carried to the various parts of the body and deposited at least in part in the fatty or lipid constituents of the cells, this agreeing with the theory of "lipotropie" advanced by Loeb. On this account the central nervous system, being rich in lipoids, is found to contain relatively much more iodine following the administration of an iodized fatty acid than after potassium iodide. After being stored in the lipoids of the cells these substances may, as suggested by Meyer and Gottlieb,³ give off free iodine when the proper conditions are present. These facts explain the longer retention in the body and the slower excretion of iodine following the administration of these preparations. The iodine is excreted in inorganic form, and probably is effective in the body only after it is separated from the organic molecule. Its action and fate after separation from the organic combination would naturally be the same as if an alkaline iodide had been administered, and the only advantage gained would be in its being held and liberated more slowly, as no one of these preparations has been shown to possess a specific action beyond that of the iodine which it liberates. The fact that relatively more iodine is found in the nervous tissues probably has little bearing on the efficiency of these substances in cerebral syphilis, etc., as their lipid solubility would not favor their entrance into syphilitic tissue. The lessened tendency to iodism claimed by many observers may be explained by the retention of the iodine in the lipoids and its slower and more uniform release in the form of available iodine. According to our present ideas iodism may be dependent on a high concentration of easily available iodine in the tissues. A high concentration may be reached for a short time by a relatively small dose of potassium iodide, but in the case of an iodized fat there is never this sudden flooding of available iodine. Where continuous small amounts of iodine are desired, as in arteriosclerosis, bronchial asthma, lead-poisoning, etc., this iodine may be supplied in a form non-irritant to the stomach as an iodized fat or fatty acid, and the probability of iodism would not be great. The iodized fats and fatty acids may be compared to the organic combinations of arsenic and mercury, in that they seem to allow to a certain extent the maximum of therapeutic effect with the minimum of toxic effect. When large amounts of iodine are desirable, however, as in cerebral syphilis, etc., the therapeutic effect seems to depend on the same property that causes the toxic effect, that is, the high concentration of iodine, and any effort to

7. Strumpell: *Deutsch. Arch. f. Nervenhe.*, 1914, 1, 455.

8. Westphal: *Arch. f. Psychiat. u. Nervenkr.*, 1913, li, 1.

* From the Department of Pharmacology, Medical Department, University of Oregon.

* Investigation supported in part by a grant from the Therapeutic Research Committee, Council on Pharmacy and Chemistry, American Medical Association.

1. McLean, Franklin C.: *Organic Iodine Preparations, their Pharmacology and Therapeutic Value*, *Arch. Int. Med.*, November, 1912, p. 505.

2. McLean, F. C.: *The Distribution of Iodine in the Cell Following Administration of Organic Iodine Preparations*, *Arch. Int. Med.*, to be published.

3. Meyer and Gottlieb: *Pharmacologie*, Berlin, 1911, p. 358.

decrease the concentration would result in a sacrifice of therapeutic efficiency.

The iodized albumins on the market are chiefly Iodalbin (P. D. & Co.) and Iodo-casein (Mulford). They are relatively unstable, and Iodalbin contains some free iodine and much more easily available iodine. Its claim for classification as an organic preparation is thus only partially borne out. As would be expected from the availability of its iodine, iodine appears in the urine within a few minutes after its administration. As I have shown² it completely loses its identity during the process of digestion and absorption, and its iodine is not found in the body in combination with protein. Any advantage of these preparations over the soluble inorganic iodides must lie in their behavior in the gastrointestinal tract. In this way they resemble the organic iron preparations, most of which are protein in nature.

It has been repeatedly demonstrated that the iron preparations are not absorbed until after digestion and that their only advantage over the inorganic preparations lies in their better tolerance by the gastrointestinal tract. In the case of iodized albumins there may be a somewhat slower absorption, owing to the time required for digestion, but their action and fate following absorption is practically that of soluble inorganic iodides.

Iothion (Farbenfabriken von Elberfeld Company) must be given a separate classification. It is chemically di-iodo-hydroxypropane, obtained by chlorinating glycerin and replacing the chlorine by iodine. It is recommended for local application and for percutaneous administration in solution in olive oil, and rapid absorption is claimed. It is apparently efficient in case percutaneous administration is desirable.

Another class of preparations, the iodized tannins, scarcely deserve classification as organic preparations. They are prepared in the form of wines or sirups, and contain tannin with a small amount of loosely combined iodine. The action of the small amount of iodine they contain is the same as the action of a corresponding amount of potassium iodide, as they decompose rapidly in the stomach.

The conclusions to be derived regarding the organic iodine preparations designed for general iodine medication are as follows:

1. So far as we now know these preparations have no specific action beyond the action of iodine after separation from the molecule.
2. The iodized fats and fatty acids, when small amounts of iodine are desired, seem to combine the maximum of therapeutic effect with the minimum of toxicity, chiefly because of their retention in the body and the slower release of the iodine. They are not of advantage when a high concentration of available iodine in the tissues is desirable.
3. The iodized proteins may be of some advantage in so far as they prevent gastric irritation and retard absorption of the iodine. Their behavior after absorption is the same as that of the soluble inorganic iodides.
4. Iothion and Iothion Oil are available for percutaneous administration, when that is desirable.
5. The sirups and wines of the so-called iodized tannins display no advantage over the soluble inorganic iodides.

761 Lovejoy Street.

INJURIOUS EFFECTS OF FORCIBLE PASSIVE MOTION IN DISEASED AND TRAUMATIC JOINTS *

ARTHUR J. GILLETTE, M.D.

Professor of Orthopedic Surgery, University of Minnesota Medical School; Chief Surgeon, Minnesota State Hospital for Crippled and Deformed Children

ST. PAUL

The terms "passive motion," "massage" and "Swedish movement" are, to say the least, very confusing in their application, they are used in such an indiscriminate way, in books of surgery, essays, monographs, clinical lectures and by the general profession. In many instances these treatments are advised regardless of the anatomic and pathologic conditions of the joints involved.

Passive motion is a different treatment from massage or Swedish movements, but all three treatments are many times suggested in such a perfunctory manner that one might regard them as the same, and the results are disastrous, especially in inflamed joints and in many forms of infected joints, as well as injuries, fractures and dislocations at or near the joints, and seldom if ever is any good accomplished in establishing normal motion. Passive motion should be abandoned in joint diseases. Personally I do not recall a case in which it has been beneficial so far as motion is concerned, by the use of forcible passive motion, *per se*.

The fact that I have advocated, pleaded and almost begged for protection and rest for inflamed joints, with Minnesota physicians, and that the opposite treatment quite frequently is practiced by the regular profession and the general surgeon, leads me to think that these recommendations are either too feeble, or not well founded. Whether or not the latter is true, will, I hope, be decided in the discussion which may follow this short paper.

Frequently too, my stiff joint patients consult medical men in New York, Boston, Philadelphia and Chicago, and return with a very courteous letter to me advising passive motion, or that the adhesions be "broken up," and this followed by forcible passive motion. Such advice, however, has never come from a strictly orthopedic surgeon. This leads me to feel that possibly the Eastern orthopedic men have similar trouble in instructing and keeping the general practitioner and the general surgeon from assaulting these unprotected inflamed and stiffened joints by forcible passive motion.

At Asheville, N. C., the past winter, a patient from Boston with stiffened and painful joints was being treated under his home doctor by passive motion. The child's nose was filled with adenoids, and his tonsils were so large that he could not speak plainly. This experience was some consolation to me, as he certainly came from a city in which he could have received much better advice, and did, but his physician failed to listen or read.

As a teacher, as a consultant, and by patients, I am sure I am asked this question more frequently than any other: "When should forcible motion be commenced in a joint in order to establish the natural movements?" The answer is, "Never forcible passive motion under an anesthetic or even active motion when it causes pain." There is always a look of surprise,

* Read before the American Orthopedic Association at Philadelphia, June, 1914.