Psychopharmacological experiments on albino rats, trained in the circular maze according to the methods of Macht and his collaborators,[1] proved that the compound produced no depression either of the central nervous system or of the neuromuscular mechanism. Phytopharmacological studies, carried out on seedlings of *Lupinus albus,* according to the methods of the senior author,[2] showed that the compound was quite toxic for plant protoplasm although it was little toxic for isolated animal tissues. This was a striking confirmation of the original findings of Macht and Livingston concerning the extreme sensitiveness of plant protoplasm to benzoates.[3]

In view of the pharmacological findings given above and the relatively low toxicity of the drug, clinical observations were justified and were made on selected cases by Dr. Keller in the orthopedic clinic, the results of which are published elsewhere.[4] Dr. Keller found that from 25 to 30 cc. of a 10% solution could be easily injected into the knee joint and gave remarkably well defined roentgenographs revealing structures and conditions around joints which could not be detected by ordinary x-ray examination without previous injections of the drug. Because of the rapid and almost complete secretion of the drug through the urinary system, carefully conducted investigations on selected urological cases are in progress under the supervision of competent genito-urinary specialists. A full description of the chemical and pharmacological studies will be published by the authors later.

5005

Experimental Studies on Visualization of Joints by Injections of a Drug.

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By the term arthritis the clinician usually means an inflammatory reaction involving the region of a joint. Such an inflammation may involve the synovial membrane alone, when it is termed more strictly synovitis. Usually, however, the inflammatory process involves the

[1] Macht and Mora, *J. Pharmacol. and Exp. Therap.*, 1920, xvi, 219.

[2] Macht and Lubin, *J. Pharmacol. and Exp. Therap.*, 1924, xxii, 413.

[3] Macht and Livingston, *J. Gen. Physiol.*, 1922, iv, 573.

[4] Keller, PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 852.

articular surfaces proper, their lining membranes, and the musculature and other soft tissues around the joints which are affected directly or indirectly by the patient's condition and play a rôle in the interference with free motion and production of pain and other symptoms. In order to institute rational treatment of a pathological joint condition, it is absolutely necessary to make a definite diagnosis and ascertain the exact condition of the tissues in the joint, or around it, which are involved, namely, whether the disease is confined to the bone itself, to the articular surfaces of the bones, or to the capsular or synovial membrane, and whether it involves the muscular tissue and has produced changes in the connective tissue, leading to adhesions. This is particularly true of the larger joints, and especially of the knee joint, which is the weakest mechanically and is subject to many diseases of acute and chronic nature leading to pathological changes. The most valuable help in the diagnosis of such pathological conditions is roentgenology, which gives a clue to the amount of involvement of bone tissue and the presence of osteophytic outgrowths in the vicinity of the joint. The x-rays, however, are not very helpful in establishing the amount of involvement of the soft tissues in arthritic conditions and, for this reason, any new method which may aid in this connection is welcomed by the orthopedic surgeon.

The author in 1914 reported experiments on the injection of phenolsulphonphthalein into the joint cavity for the purposes of determining the absorptive power of the joint.[1] Such experiments on the permeability of the synovial membranes have recently been repeated by Curtis and Brunschwig,[2] who have seemingly overlooked the previous work on the subject and made no reference to the paper mentioned above.

In connection with experiments on the injection of phenolsulphonphthalein into the joint cavity, the writer attempted to inject a dye or some other suitable drug into joint cavities to increase the usefulness of x-ray examinations. The ideal conditions for a substance used in such a manner are: (1) it must be comparatively non-toxic; (2) of sufficient density to cast a marked shadow with the x-rays; (3) easily injected and produce the minimum amount of local irritation; (4) easily eliminated a short time after injection. A number of dyes and chemicals have been tried, most of them, however, unsatisfactory. Finally, a new chemical compound, neu-

[1] Keller, Henry, *New York Med. J.*, September 5, 1914.

[2] Curtis, G. M., and Brunschwig, A., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 358.

tral sodium salt of tetra-iodo-ortho-sulpho benzoic acid, prepared by the chemist, Dr. Daniel Twiss, and investigated pharmacologically by Dr. David I. Macht, of Baltimore, was found to fulfil all requirements. This compound is a bright yellow crystalline powder, easily soluble in water, a 10% solution of which is nearly isotonic with blood serum. The compound has a molecular weight of about 750 and its iodine content is 67%. A complete study of the substance is published by Macht and Twiss elsewhere in this journal.[3]

Using a sterile 10% solution of this drug, the writer has performed experiments, first on dogs, by injecting the solution into the joints, and found that the drug was non-irritating and produced sharply defined shadows, giving a clear picture of the joint cavity with the x-ray. The comparatively low toxicity of the drug having been established by Dr. Macht, solutions of the drug were then cautiously administered for diagnostic purposes to selected patients. The results obtained were very satisfactory. It was found that from 25 to 30 cc. of the 10% solution could be easily injected into the knee joint, and such joints, when examined with x-rays, gave information concerning the condition of the bone surfaces, presence of osteophytes and foreign bodies, and the degree of involvement of the soft tissues not obtainable by a simple x-ray examination. The injection of the tetra-iodo-ortho-sulpho benzoate was found to be particularly useful in detecting the presence and extent of adhesions in and around the joints, especially the knee joint. Injections of the drug did not produce irritation but in some cases mild reactions followed several hours later which, however, did not last long and such reactions in several of the patients led to an improvement in the arthritic symptoms so that the patients desired another injection. It is hardly necessary to add that all the usual surgical and antiseptic precautions must be observed in inserting the needle and making injections into joint cavities. A resumé of the following cases will give an idea of the results obtained. A full account of the experimental and clinical work will be published elsewhere.

Case I. A. K——, aged 40 years, Greek, female. Chronic arthritis of right knee, synovial type. Wassermann negative. Physical examination negative except for right knee. Prior to injections of drug, x-ray examination, anterior-posterior view, showed clear interarticular surface with slight irregularity of inner and upper end of tibia. Lateral view revealed same picture. In popliteal region of knee joint there seemed to be a thickened synovial fold with

[3] Macht, D. I., and Twiss, Daniel, PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 850.

lime deposits. Injection of 25 cc. of sodium tetra-iodo-ortho-sulpho benzoate, 10% solution, gave the following x-ray findings. Anterior-posterior view: the dye penetrated capsule and synovia over three-quarters of the joint cavity on fibular side; the inner quarter, however, was entirely free from the presence of the opaque drug. Lateral view: the drug invaded all but the popliteal surface and there was also some mid-portion of the capsule lighter than the rest of the joint cavity, thus pointing to the presence of adhesions. Injection of phenolsulphonphthalein showed absorptive integrity of the joint to be good. The patient had a mild reaction after the injection, which cleared up.

Case II. W. S——, aged 56 years, male, admitted to Neurological Hospital with diagnosis of lues, cerebrospinalis and Charcot's ankles, the right being more involved than the left. Wassermann positive. Lange's colloidal gold test positive. Ordinary x-ray examination confirmed diagnosis of Charcot's disease of the ankles. Twenty-five cc. of 10% solution of yellow dye were injected into right ankle joint. The fluid went in with some difficulty. X-ray examination soon after did not show marked change in contour but the line of demarcation of the debris was more distinct. The loose bodies did not seem to be displaced. The findings, therefore, indicated the presence of loose bodies in the ankle joint, seemingly firmly imbedded in the organized soft tissue exudate. A subsequent operation confirmed the x-ray findings made after injection of the drug.

5006

Mucosal Inclusions in Anterior Gastroenterostomies in Dogs Following Various Methods of Suturing.

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(Introduced by George E. Burget.)

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The object of this study was to ascertain how healing progressed in anterior gastroenterostomy wounds in dogs when the techniques of suturing employed were similar to those commonly used. The duodenum was sutured to the anterior stomach wall in 50 dogs. The animals were sacrificed by chloroform inhalation after 6, 9, 14, 20, and 27 days. The stomach and duodenum were removed at once