

to secrete a sufficient amount of estrogen to produce genital development and endometrial growth, and, second, that in which the ovaries, based on blood estrogen determinations, are apparently functioning normally, but owing to some inherent defect in the müllerian duct system normal estrogenic stimulation does not produce uterine growth and bleeding. It is in the last condition that large dosages of estrogen are necessary.

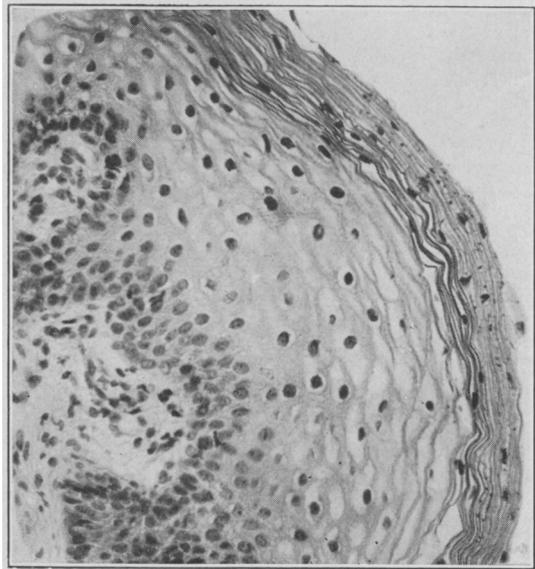


Fig. 4.—Vaginal wall of castrate 2 after injection of 5,000 international units of theelin in oil.

The fourth question to be answered was the effect of different dosages of theelin in oil on the breasts, on the visible parts of the genitalia, on the endometrium, on the vaginal mucosa and on the vaginal secretions.

This question has been answered under the gynecologic report. The effect of theelin in oil on the endometrium and vaginal mucosa is shown in the accompanying illustrations and is described in the report on the histologic and vaginal smear examinations.

CONCLUSIONS

1. Theelin in oil stimulates development of the sex-related structures of the human female, producing changes in the breasts, gross appearance of the vagina, with increased mucous secretion, and growth of the endometrium and vaginal mucosa in dosages as low as 5,000 international units.

2. Definite changes in the vaginal smears were noted with dosages of theelin in oil as low as 10,000 international units. Vaginal smears would appear to be a less delicate index of theelin administration than uterine mucosal specimens. Relief of symptoms of castration was obtained with dosages as low as 5,000 international units, which is insufficient to produce the full follicular phase in the vaginal smears.

3. This experiment proves that dosages of 5,000 international units of theelin in oil, when the element of time is considered, will mitigate or relieve the symptoms of castration but at the same time will stimulate development of the endometrium sufficiently to cause uterine bleeding when discontinued.

4. Theelin in oil is much more effective than theelin in aqueous solution. When administered intramuscularly in the human being, smaller dosages and less frequent intervals of injection produce more rapid and more marked effect on the endometrium and vaginal mucosa.

5. The evidence seems conclusive that the large dosages of theelin advocated by some (from 30,000 to 50,000 rat units) as necessary to produce the interval phase of the endometrium are grossly excessive.

404 Humboldt Building.

A TREATMENT FOR SUBLUXATION OF THE TEMPOROMANDIBULAR JOINT

LOUIS W. SCHULTZ, D.D.S., M.D.
CHICAGO

Subluxation of the temporomandibular joint is fairly frequent. Its causes include congenital weakness of the capsule or malformation of the condyles or both. The joint may be strained or injured during general anesthesia, yawning, attempts by children to insert large objects into the mouth, and positional pressures during sleep.

Heretofore the usual treatment has been merely rest. To safeguard a subluxating joint from undue motion for one whole year by bandaging is obviously impos-

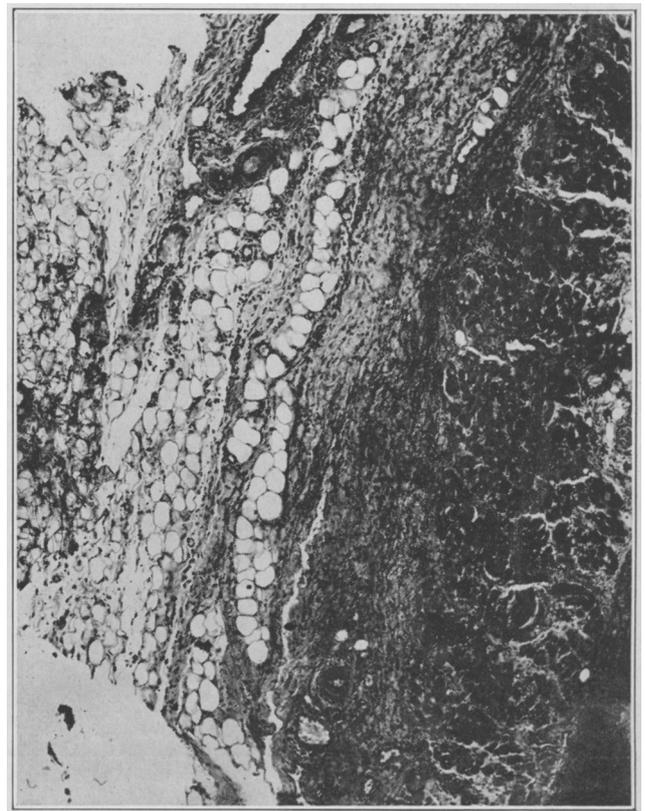


Fig. 1.—Section of subcutaneous tissue of dog three days after the injection of sodium psyllate, showing the subacute reaction with infiltration of lymphocytes.

sible. Surgical treatment has been attempted with some success by the use of mattress sutures inserted laterally through the capsular ligament or by the removal of the

From the Department of Surgery, University of Illinois College of Medicine, the Illinois Research and Educational Hospital and the Department of Public Welfare.

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Prof. Otto F. Kampmeier, head of the department of anatomy in the University of Illinois College of Medicine, placed the facilities of his laboratory at the author's disposal, and Walter Shriner, M.S., M.B., senior medical student, abstracted the bibliography and helped in the animal experiments.

meniscus. Physical therapy has been employed. Orthodontic appliances and prosthetic devices, pressure pads in front of the ears held in place for several months by a steel spring passing over the calvarium, wiring the jaws in occlusion and bandaging the jaws for months at a time—all these have been tried and found only partially successful. Changing the bite has been and is practiced with some success when that is the cause.

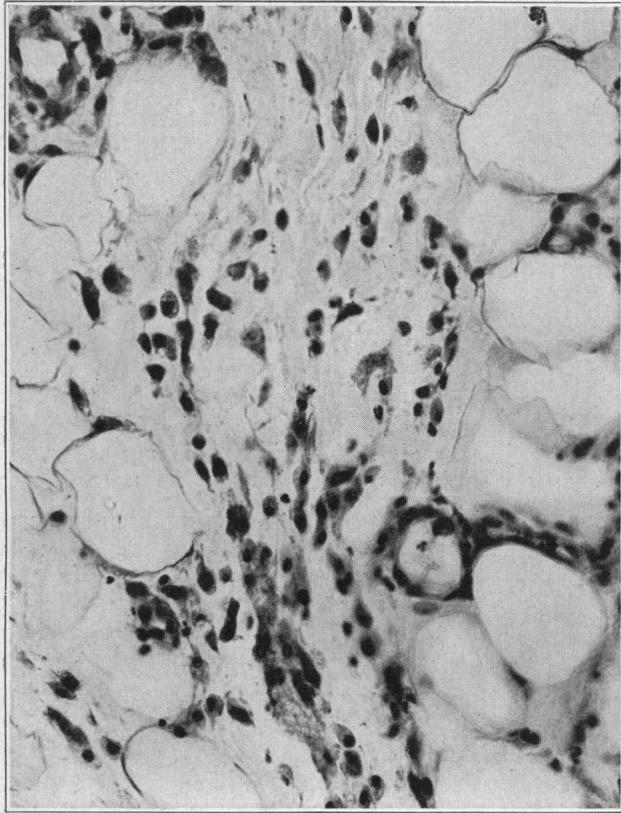


Fig. 2.—More highly magnified section of subcutaneous tissue of dog three days after the injection of sodium psylliate, showing the transition of lymphocytes (?) into fibroblasts.

I have developed a simple method of shortening and strengthening the capsule of the joint by injection. Fibrogenesis in the capsule of the joint is the result to be attained.

Pendse and Dutt¹ of India carried out extensive investigations with regard to the chemistry of the seed of psyllium or *Plantago ovata*. They found that the seed has a large content of mucilage but does not contain any alkaloids or glucosides.

ANIMAL EXPERIMENTATION

In view of Rice's² results with various sclerosing solutions, I decided to test some of the reagents, among them sodium psylliate,³ on the temporomandibular joint. Sodium morrhuate, thuja solution and Mayer's solution were some of the other substances tried. I shall present only the results obtained with sodium psylliate and the technic of employing it.

The agent used must not be injurious to the joint or surrounding tissues, the therapeutic response should be painless, the solution should not be injurious if, by

1. Pendse and Dutt: Proceedings of the Academy of Science (United Provinces Agra Oudh, India) 4:133, 1934; Chem. Abstr. 29:7577, 1935.

2. Rice, C. O.: Injection Treatment of Hernia, Philadelphia, F. A. Davis Company, 1937.

3. Furnished by the courtesy of G. D. Searle & Co.

chance, it enters the veins, the degree of fibrogenesis should be controllable, and no untoward systemic reaction should follow.

Considerable experimentation was necessary to find the most effective fibrosing agent. Figure 1 shows the subacute reaction in normal subcutaneous tissue three days after the injection of sodium psylliate. Figure 2 portrays a more highly magnified section of such tissue, illustrating more particularly the transformation of lymphocytes into fibroblasts.

A series of from eight to ten injections per dog made every two weeks showed all joints in perfect functional and anatomic condition at autopsies made at biweekly intervals on this series of dogs. Cartilage surfaces were smooth and glistening, as was the synovial membrane (fig. 3).

In all injected joints the capsules averaged from 5 to 7 mm. more in thickness than in the control specimens.

Twelve dogs were given injections of from 1 to 2 cc. of sodium psylliate into the temporomandibular joints at biweekly intervals for three months. Under deep anesthesia the opening between the incisor teeth was measured on each occasion. A loss of from 3 to 5 per cent of the original opening was noted. Autopsy revealed normal joint cavities with a firm, fibrous capsule in all dogs.

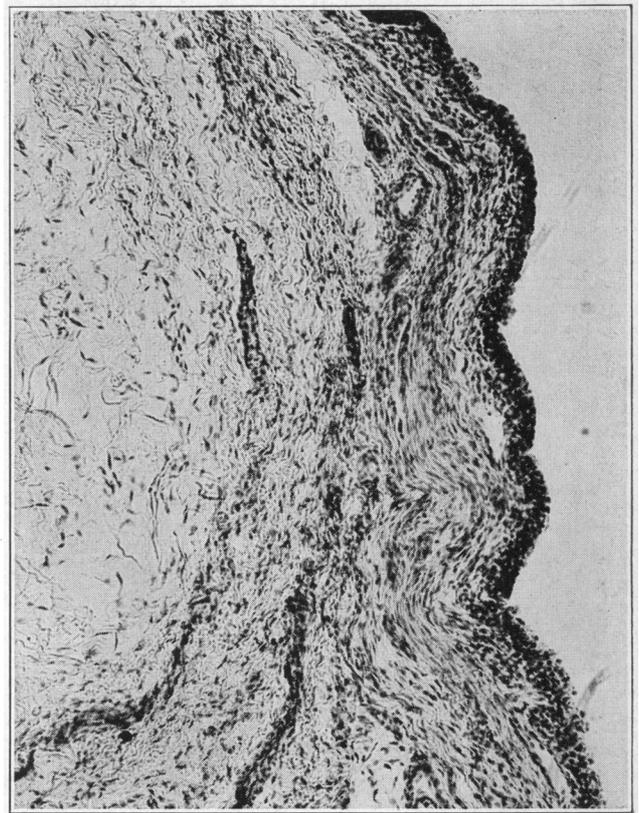


Fig. 3.—Section of synovial membrane of dog fourteen days after the last of eight injections of 1 cc. of sodium psylliate at biweekly intervals; it shows no evidence of a destructive process.

Results of other experiments are as follows:

1. Subcutaneous injections (from 5 to 20 cc.) were made. In from two to three weeks large areas of firm fibrosis resulted, with no discomfort and with no sloughing.

2. From 1 to 2 cc. of sodium psylliate injected into firmly healed, abdominal scars caused a small area of necrosis.

3. Injections of from 1 to 2 cc. of sodium psyllate into the mental and infra-orbital foramina produced no effect. Motor nerves were tested with a similar absence of effect.

4. Injections of from 60 to 120 cc. into the peritoneal cavity produced no effect either immediately or subsequently, as proved at autopsy from one-half to three months later.

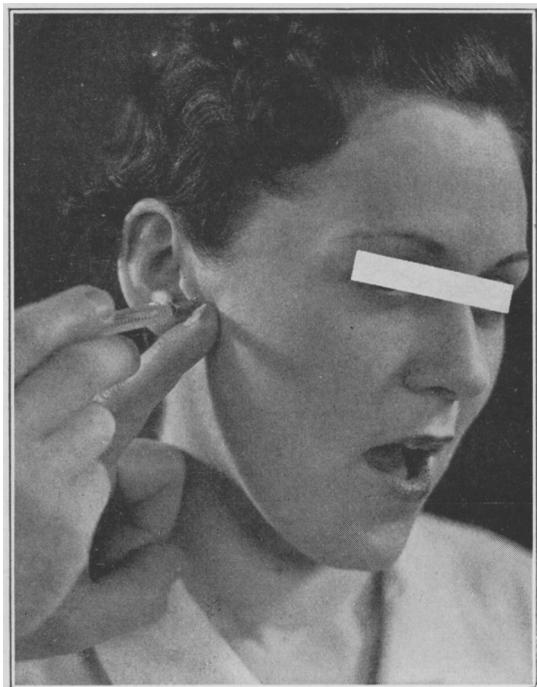


Fig. 4.—Technic of injection of temporomandibular joint.

5. Introduction of this agent into normal pleural cavities showed no gross effect on the pleura or lung at autopsy.

6. Five cc. put into the gallbladder produced a firm generalized fibrous sheet over the immediately adjacent liver and over the biliary apparatus but had no other effect. The amount of fibrous tissue varied considerably in these dogs.

7. From 30 to 60 cc. injected directly into the left ventricle of the heart on three successive days and at weekly intervals revealed no effect either immediately or at autopsy.

8. Scarifying and coating with sodium psyllate of stomach, intestine and liver and introduction of about 30 cc. of the solution into the peritoneal cavity produced no adhesions in from two weeks to two months, as shown at autopsy.

Many hundred celloidin sections of the tissues subjected to the action of sodium psyllate were made and examined, all of which showed fibrogenesis, as indicated in the foregoing narrative.

In brief, the animal experiments demonstrated that:

1. There was no alteration of the joint cavity, the fibrosis occurring in the ligaments.

2. There were no gross changes in the ligaments other than their thickening, and hence the strengthening of the chief factors that hold the joint within its cavity.

3. Subacute reaction followed thirty minutes after the injection of sodium psyllate.

4. There was infiltration of leukocytes at this time.

5. Two or three hours later a lymphocytic infiltration starts.

6. Fibrosis of this tissue starts in from four to six days.

7. Injections into the joint cavity caused some discomfort.

8. Large doses injected directly into the blood stream were followed by no symptoms.

9. Injections into the heart produced no recognizable effects.

10. No infection followed the treatment.

CLINICAL APPLICATION

The harmlessness of treatment with sodium psyllate and the quick results obtained convinced me that it was the agent of choice for my purpose.

Injection is made only after a complete history is obtained, including examination of the joint, the external auditory meatus, the drum head and the occlusion of the teeth. If indicated, the procedure is as follows: The ball of the index finger is placed in front of the tragus, and the patient opens the mouth wide enough to cause the head of the condyle to subluxate, "click," or produce abnormal movement of the fibrocartilaginous disk. The needle is inserted into the joint cavity (fig. 4) and from 0.25 to 0.5 cc. of the solution is deposited inside the joint cavity. The injections are repeated weekly or biweekly on both joints until a sufficient

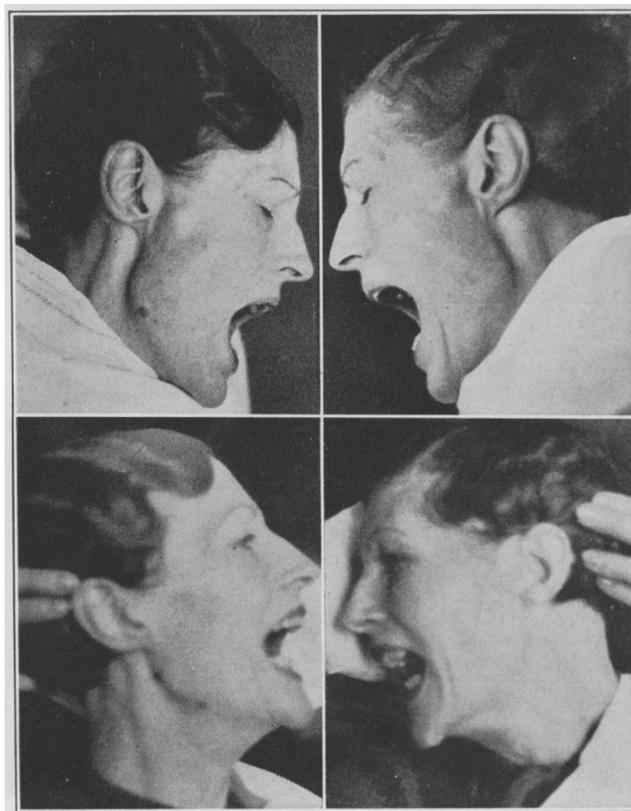


Fig. 5.—Above: patient before injection. Note great protrusion of condyles. Below: one week after the first injection of sodium psyllate. Both condyles are in position.

fibrosis is obtained. This occurs usually in from three to five weeks. The injections, therefore, number from three to four at the intervals stated.

The technic of injection should not produce more disturbance than the prick of the needle and a slight feeling of fullness at the time of the injection. Pain usually follows twenty or thirty minutes later, at which

time the patient may be given a sedative, or an anodyne may be applied to the parts involved.

Since the area to be treated contains many important structures, such as the internal maxillary and internal carotid arteries, the middle and internal ear, the brain, the parotid gland and the facial nerve, the course of injection should proceed with due caution.

During the past year I have treated more than thirty patients afflicted with temporomandibular subluxation by the method described, with results that approach entire satisfaction. Figure 5 illustrates the condition presented in one of these patients and the results attained.

It appears logical to assume that the principle herein described, namely, thickening and shortening of the joint capsule by injection of a fibrosing agent, might be applied therapeutically to other joints. It is probable that the lesions of other joints most apt to be amenable to this form of treatment would likewise be subluxation or partial dislocation, although it is barely possible that even recurring complete dislocations might respond favorably, particularly if numerous injections were performed.

CONCLUSIONS

1. Stabilization of joints by injection therapy is successful.
 2. Sodium psylliate is a dependable fibrosing agent.
 3. Sodium psylliate is noninjurious to tissues generally.
 4. In experienced hands it is relatively harmless, and office therapy is possible.
 5. It produces no apparent systemic disturbances even when injected intravenously into animals.
 6. The fibrosis obtained by the injection of the temporomandibular joint for subluxation persists long enough to restore the joint to normal function.
 7. The method of treatment comes within the scope of the general practitioner.
- 25 East Washington Street.

Clinical Notes, Suggestions and New Instruments

PURPURIC AND SCARLATINIFORM ERUPTION FOLLOWING SULFANILAMIDE

IRVING L. SCHONBERG, M.D., CLEVELAND

Since the advent of sulfanilamide as a therapeutic agent there will no doubt be many reports concerning reactions. The following is of clinical interest because of the fact that a toxic purpura first developed, which appeared following the use of sulfanilamide and recurred one month later as a scarlatiniform eruption as a result of a smaller dose of the same medication.

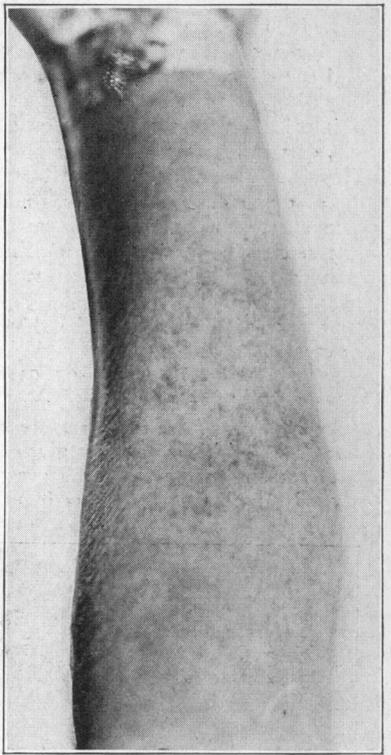
REPORT OF CASE

A. G., a Jewish woman, aged 21, presented an erysipeloid dermatitis involving the vulva and extending to the adjacent surface of the thighs and also into the left inguinal area. The vulva presented a marked edema, considerable erythema and some vesiculation. The skin was infiltrated and tender, and there was increased local temperature. The edema was non-pitting. The areas were sharply demarcated and slightly raised above the adjacent skin. The temperature was slightly elevated (100 F.). An acute adenitis developed and it was necessary to incise the inguinal gland. Cultures were made from a thin serosanguineous fluid which exuded from the sinus, and streptococci of the hemolytic type were found. The local treatment consisted of wet dressings of 1 per cent zinc sulfate-copper

sulfate solution. The inguinal sinus was douched with 1 per cent gentian violet solution. Drainage persisted for some time and the sinus failed to heal. There were recurrent attacks of edema and erythema of the vulva.

In view of the fact that streptococci were found on culture, it was deemed advisable to administer sulfanilamide. The usual dose of four 5 grain (0.3 Gm.) tablets every six hours was administered the first day and two tablets every six hours on subsequent days. On the fourth day an eruption developed over the entire body, which was at first composed of erythematous wheals and macules. The temperature rose to 104 F. The drug was discontinued but the eruption progressed. Finally the urticaria disappeared and the patient presented a generalized purpuric rash composed of purplish macules that did not fade on pressure. Supportive treatment eliminated the purpuric eruption within a few weeks. The sinus healed and the edema and erythema of the vulva subsided completely.

One month later an edema of the vulva again developed, which, although not as marked as the original condition, was similar in appearance. At this time there was a right inguinal adenitis. One 5 grain tablet of sulfanilamide was administered and four hours later a generalized scarlatiniform eruption developed. No distinct lesions of any type were present. The patient in addition suffered an acute edema of the eyelids, the lips, the larynx and the forehead, considerable difficulty in breathing, pain in the chest and a temperature again elevated to 104 F. Pruritus over the entire body was intense. Twenty-four hours later the temperature had subsided, the eruption was faint, and breathing was normal.



Purpuric eruption on right forearm after administration of sulfanilamide.

SUMMARY

This case illustrates that sulfanilamide is another drug which exhibits allergic manifestations. This patient, in whom a purpuric rash first developed following its use, presumably developed a hypersensitivity of her entire organism, so that one 5 grain tablet precipitated marked allergic symptoms. Extreme caution is advisable in resuming the use of the drug following any type of skin eruption. Fortunately the patient did not take more than one 5 grain tablet. A larger dose would probably have provoked a condition of extreme gravity.

524 Keith Building.

Interest in the History of Medicine.—Dr. Garrison's position in American medicine is unique. No one prior to his time had stimulated so widespread an interest in the history of medicine, or reached into the consulting room and library of every serious student and practitioner in the United States. In the minds of American physicians from 1913 on, Garrison and medical history became synonymous; Garrison's "Introduction to the History of Medicine" became their chief source-book.—Viets, H. R.: Fielding H. Garrison and His Influence on American Medicine, *Bull. Inst. Hist. Med.* 5:347 (April) 1937.