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**EXPERIMENTS WITH EMULSIONS
OF ORGANS TAKEN FROM THE
DEAD HUMAN BODY AND
SEX-GLANDS OF THE
LOWER ANIMALS.**

65496

BY

G. FRANK LYDSTON, M. D.,

Formerly Professor of Genito-urinary Diseases
and Syphilology, Medical Department, State
University of Illinois, Chicago, Ill.

In connection with my recently reported series of experiments in the implantation of sex-glands taken from dead human bodies,¹ I made brief reference to certain experiments I had been making with emulsions of tissues from dead human donors. The purpose of present paper is to record these experiments in more comprehensive form.

The idea of the tissue emulsion experiments was based upon the following, viz.:

1. (a) Dr. Leo Loeb's experiments

¹ Implantation of the Generative Glands and Its Therapeutic Possibilities, *N. Y. Med. Journ.*, Oct. 17, 24, 31 and Nov. 7, 1914.

[Reprinted from *American Medicine*, New Series, Vol. IX, No. 12, pages 767-773, December, 1914.

showing the feasibility of cultivating living tissue cells both *in vivo* and *in vitro*.²

(b) The fact that cell death is not synchronous with somatic death.

2. The belief that, even granting the efficacy of tissue extracts, fresh tissue emulsion, if it be practicable to employ it, should be far more reliable.

3. The results of my own experiments in implantation upon the living of organs derived from somatically dead donors.

4. The belief that tissues and organs taken from healthy dead human bodies are not only safe for use upon the living, but far more logical in therapy than are preparations of any kind made from the lower animals.

5. Disbelief in the alleged dangers of anaphylaxis—by virtue of the injurious action of the proteid—in using organic tissues or juices from alien sources, dead or living.

6. The suspicion that every non-glandular, as well as glandular tissue, forms a nutritive stimulant and defensive metabolic product of a degree of specialization and

² Johns Hopkins Hospital Bulletin, 1898, Proceedings of the Society of Experimental Biology and Medicine, VIII, 1911, and Anatomical Record, VIII, 1912.

Loeb's experimental results were the pioneer indices of everything that since has been done in tissue transplantation. The distinguished scientist has not received the credit due him at the hands of certain investigators, with whom scientific enthusiasm is submerged in the desire for personal prestige.



potency directly proportionate to the degree of specialization of the organ tissue itself. Such a metabolic product naturally might be expected to have a special action upon the nutrition in general, and a special action upon the organ which produces it, or upon the same organ in other subjects. The idea of a highly specialized metabolic product is in a measure substantiated by Abderhalden's theory of the specially differentiated albumen molecule as a basis for organ function.

In a recent interesting article on the mechanism of immunization by Williams and Beveridge appears the following: "The mechanism which gives the human organism partial or complete immunity against bacterial disease, comprises what may be called the cytogenic system—including lymphatics, bone marrow and spleen—with its daughter cells, the white and red blood corpuscles, as its active agents, and with the liver as the excretory organ of the waste products incidental to the immunizing process.

"This theory assumes that the entire cellular system of the organism—viscera, muscles, brain—may be considered as a secondary apparatus, standing, as it were, in the background, ready to supplement the work of the chief immunizing agents. So general an implication as the latter may

seem to savor of the nature of a truism; but it will appear that the theory ascribes a specific and definite part in the immunizing process to the body-cells, in general and in particular, attempting to trace the precise rationale of their activity. Equally specific is the interpretation of the activities of the leucocytes and the red blood corpuscles, which are deposited as the chief and controlling mechanism in the process of immunization."¹

The foregoing theory has a direct bearing upon the possible therapeutic uses of organ emulsions.

All experimental emulsions were kept refrigerated, but not frozen. As the emulsions were not only refrigerated, but prepared with tri-kresol, the possible danger of syphilis was not seriously considered. Experiments with all emulsions were first made upon the guinea-pig.

The first experiment was with kidney tissue removed from the body of a man dead twelve hours from contact with a live wire, and from which I had an emulsion prepared with isotonic salt solution, and as concentrated as was compatible with injection via a No. 20 needle. The entire tissue was used. Lest the criticism be made that the tissue was of doubtful vitality because

¹ The Mechanism of Immunization, Drs. Henry Smith Williams and James Wallace Beveridge, AMERICAN MEDICINE, Oct., 1914.

of death by the electrical current, I would refer the reader to my gland implantation experiments, in which testes removed from bodies dead from electricity were successfully used. In one instance an entire testicle was successfully used from the same body from which the kidney under consideration was removed. In another case a portion of testes from the same donor was used.

EXPERIMENTAL SERIES A.

Human kidney emulsion. 12 grams of kidney tissue in 4 cc. of isotonic salt solution. Tri-kresol, .2%, added as a preservative. Injection made intraperitoneally. Dosage 1 cc.

Preliminary cultures made of emulsions—no growth.

1. First pig—1 cc. injected, showed some orchitis, disappearing second day. No other reaction.

2. Second pig—1 cc. injected every other day for ten days. No reaction of any kind. Pig in good condition. Ate well. After an interval of three days pig was given another injection. No reaction. Another injection given again in 5 days. No reaction. Another injection given again in 10 days. No reaction.

Pigs soon after were used as complement in Wassermann tests. They proved exceptionally good.

The "orchitis" in the first pig doubtless was due to traumatic irritation of the intrapelvic portion of the spermatic cord, and probably was associated with a more or less marked inflammation of the peritoneum covering the cord, merely as a result of traumatic "insult."

Following the foregoing experiments I injected subcutaneously upon my own person,

in the anterior aspect of the thigh, for one week, a daily dose of 3 cc. of the kidney emulsion. No harmful effects resulting, I submitted the remaining portion of the emulsion to my friend Dr. J. L. Smith, who, administered it to a case of chronic nephritis in its last stages. The dosage was the same as employed upon myself. Four daily injections were given. No result of any kind was noted, the remedy, if ineffective, apparently being harmless, which observation, so far as it goes, is at least encouraging to future experimentation.

EXPERIMENTAL SERIES B.

Human brain and medulla emulsion. Isotonic salt solution. .2% tri-kresol.

The history of this particular brain is most interesting. It was removed from the body of an apparently healthy man of thirty, dead about eleven hours of an accidental fall. The brain was removed with the ordinary post-mortem instruments, with no anti-septic precautions, by a medical friend who was not aware of the purpose for which I had requested him to procure the organ. It was placed in a dirty, rusty pan, covered with a newspaper and allowed to remain in an undertaker's morgue awaiting my disposal. As it was a hot July day, the prospects of satisfactorily using the brain for emulsion experiments seemed, on my arrival four hours later, a trifle unpromising. I took

the organ to my office, however, washed it thoroughly in cold water, and placed it in a pitcher of solution of chinosol, 1-2000. Four hours later it was sent to the laboratory, removed from the chinosol solution and placed in normal salt solution. As will be noted, the emulsions made from this brain were sterile, thanks, I believe, to the chinosol, which is not only an excellent antiseptic but seemingly has the merit of preserving tissue without destroying it. The test of the drug certainly was a severe one.¹

- A. Emulsion of medulla.
Cultures made—no growth.
Aug. 4th.—Guinea-pig injected 2 cc.—no reaction.
Aug. 5th.—Guinea-pig injected 2 cc.—no reaction.
Aug. 6th.—Guinea-pig injected 2 cc.—no reaction.
- B. Emulsion of cerebellum.
Cultures made—no growth.
Aug. 4th.—Pig injected 2 cc.—no reaction.
Aug. 5th.—Pig injected 2 cc.—no reaction.
Aug. 6th.—Pig injected 2 cc.—no reaction.
- C. Emulsion of cerebrum.
Cultures made—no growth.
Aug. 4th.—Pig injected 2 cc.—no reaction.
Aug. 5th.—Pig injected 2 cc.—no reaction.
Aug. 6th.—Pig injected 2 cc.—no reaction.

At the conclusion of the laboratory experimentation, I injected in my own person daily for ten days, in the anterior aspect of the thighs, doses varying from 3 to 6 cc., using the cerebral emulsion. No effects were noted, save a little soreness and swelling for

¹ Note in this connection Seiffert and Hüne, Gewinnung Keimfreier Lymphedurch Zusatz von Chinosol. Cent. f. Bakt., 1913, vol. 71, p. 86.

a day or two with a little redness of the skin in several of the injected areas. Simultaneously with the auto-experimentation, I administered intramuscularly the cerebral emulsion to a medical friend of seventy years of age who was suffering with profound and obstinate "neurasthenia." Incomplete observations on the blood, blood-pressure and urine were made in this case. No physiologic results were noted, but there was a marked change for the better in the subject's physical condition, which possibly would have been greater had there not existed unavoidable causes for mental worry. As to whether or not the change for the better was due to the treatment, this, of course, is an open question.

In a case of a healthy subject to whom I daily administered 6 cc. doses of cerebellar emulsion intramuscularly in the gluteal region—the point of administration in all the cases except myself—there were no results save that the patient stated that an erection and nocturnal emission followed the first dose; these phenomena not having previously occurred for the preceding ten months. In a number of other practically healthy subjects similarly treated, nothing of the kind was noted.

In all, I administered the brain and medullary emulsion to ten subjects. In none were there any adverse results. Several of

the subjects expressed themselves as invigorated and as having an increase of appetite. There was no psychic element in the results other than that attendant upon any kind of treatment, as the precise nature of the "medicine" was not confided in any instance. In several cases, following the full dose of 6 cc. there was some muscle soreness with a slight rise of temperature—.5 to 1.°. As a rule, no special soreness at the site of injection was complained of.

At my request Dr. Geo. Leininger, superintendent of the Chicago State Hospital, instituted a series of observations of the effect of the emulsions. His results are set forth in the following letter:

"Dunning, Ill., Oct. 26, 1914.

"Dr. G. Frank Lydston,
32 N. State St.,
Chicago, Ill.

Dear Doctor:—

I am sending you a short summary of our results with patients who were given injections of cerebral and cerebellar emulsions. Eight patients in all were treated. Six of these were diagnosed as dementia praecox, including the catatonic, hebephrenic and paranoid types. One epileptic and one paretic also were given the injections. In only one of these cases, the epileptic, was there an increase of about 4,000 leucocytes. Only one patient showed temperature changes and this was a case of paresis, temperature going up as high as 102, rectal. This was after the third injection that the patient received, other times 100 and 101.

Two of these patients showed some improvement, although the nature of their illness makes it very unsatisfactory as one was a catatonic who was in a stuporous condition and the other, a paranoid dementia praecox case, who had not been eating well but who started to eat and

since that time has been in a very good condition. The initial dose in each case was 4 to 4½ cc. These were increased in some of the cases up to 6, 7 and 8 cc. However, as the amount of the material was small, it was not possible to give larger doses. All received at least 8 doses and from that amount up to as many as 20. Summarizing will say that the only temperature rise was in the paretic, a condition which is not uncommon among these patients and probably was not due to the injections. One cannot account for the increase of the leucocyte count, other than it was due to the injection.

The improvement in the two cases noted, may or may not have been due to treatment but one would hesitate to say that it was due to the treatment, because it was naturally supposed that these two cases would improve.

We wish to thank you very much for the material which you gave us and we are very glad that we were given the opportunity to use this and certainly appreciate your interest in this line of work.

Yours respectfully,
(Signed) GEO. LEININGER, M. D.,
Superintendent."

Comment upon the foregoing, save to agree that an increased leucocytosis naturally should follow full doses of the emulsion, would be superfluous. I wish to state, however, in passing, that I am under the deepest obligations to Dr. Leininger for many courtesies and for co-operating with me, under very adverse conditions, and at great inconvenience to himself in all my experimental work. In this work of co-operation, Dr. Leininger's efforts have been ably supported by a staff of hospital assistants which is second to none in this country in earnestness of purpose and enthusiasm.

EXPERIMENTAL SERIES C.

Human spleen emulsion. Isotonic salt solution .2%. Tri-kresol.

Cultures made—no growth.

(1) Oct. 13th.—1 cc. injected into peritoneal cavity of pig—no reaction.

Oct. 14th.—1 cc. injected into peritoneal cavity of pig—no reaction.

Oct. 15th.—1 cc. injected into peritoneal cavity of pig—no reaction.

Oct. 16th.—1 cc. injected into peritoneal cavity of pig—no reaction.

Pig in good condition, eats well.

Pig killed and successfully used for Wassermann complement.

(2) Guinea-pig injected, inner aspect of thigh, with 1 cc. human spleen emulsion daily for five days. A few small nodules size of sage grains formed at site of injection under skin. Pig was killed and successfully used for Wassermann complement. Autopsy showed slight hyperemia of lower lobes of lungs, anemia of the liver and spleen and injection of cortex of kidneys. Otherwise normal.

Injections of from 3 to 6 cc. were given daily for a week to three healthy human subjects. The only result noted was an apparent loosening of the bowels, for several days in one case. Three subsequent cases were more suggestive.

1. A man forty years of age, suffering from constipation, but otherwise in practically perfect health, stated that his bowels moved only once in two or three days, and then only with cathartics. After two injections of 6 cc. of the splenic emulsion on two successive days, the bowels moved normally and freely every day for one week. Constipation recurring, a second dose was given, with satisfactory results lasting six days,

when a third dose was found necessary. Since the third dose, a period of three weeks, the bowel movements have been daily and normal.

2. A man twenty-five years of age had suffered for some months from constipation. A single dose of 6 cc. of splenic emulsion resulted in daily movements of the bowels for six days. The bowels again became sluggish and 4 cc. of liver emulsion were administered, apparently with excellent results for twelve days, when the patient ceased to report.

3. A man twenty-eight years of age under treatment for prostatitis had been constipated for several weeks. A single dose of 6 cc. of splenic emulsion was followed by daily movements for one week.

EXPERIMENTAL SERIES D.

Human pancreas emulsion. Isotonic salt solution. .2% tri-kresol. Guinea-pig injected.

Oct. 13th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 14th.—1 cc. emulsion injected into peritoneal cavity—pig complained, sat in corner moaning.

Oct. 15th.—1 cc. emulsion injected into peritoneal cavity—complained.

Oct. 16th.—1 cc. emulsion injected into peritoneal cavity—complained.

Oct. 19th.—Pig evidently dying and was chloroformed.

Pig was satisfactorily used for Wassermann complement. Autopsic findings:

Generalized hemorrhage and fibrinous peritonitis, hyperemia of lower lobes of lungs, hyperemia of cortex of kidneys, thrombus on mitral valves.

The peritonitis in this pig was so obviously due to serious traumatic injury at the time of injection of the emulsion into the peritoneal cavity, that I did not regard it as indicating any danger from the proper use of the emulsion in the human subject, or even in the guinea-pig. Another pig was subjected to a similar series of injections in the inner aspect of the thighs, with no untoward result. The animal was killed and successfully used for Wassermann complement. Autopsy showed nothing abnormal save edema of the left thigh and slight diffuse hemorrhagic infiltration of the right thigh from the last injection given. After administering to myself three daily doses of 3, 4 and 6 cc. respectively, I gave a series of seven daily gluteal injections of 6 cc. to a woman of sixty years of age, who was under treatment for syphilis of long standing. A blood count was made in this case, and an increase of leucocytes from 6,000 to 8,000 was noted on the third day. The leucocytosis gradually disappeared after the fifth injection. No other effect was noted.

EXPERIMENTAL SERIES E.

Human liver emulsion. Isotonic salt solution, .2% tri-kresol. Cultures made—no growth.

Guinea-pig injected.

Oct. 13th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 14th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 15th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 16th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Pig in good condition, eats well.

Pig killed and used satisfactorily for Wassermann complement. Area of localized peritonitis at site of injection, diameter 2 cm. Old infarcts, (2) in liver and (2) in lungs. Hyperemia of lower lobes of lungs. Hyperemia of vessels of heart.

Intestinal peritoneum normal; no puncture of intestines.

The liver emulsion was tested on four human subjects, without untoward results. No tests of the action of any of the human emulsions in disease were made, excepting in the cases of constipation already recorded.

Desiring to make a more severe test of the safety of tissue emulsions I decided to employ alien organs and procured a quantity of testes of young rams.

EXPERIMENTAL SERIES F.

Ram's testicle emulsion. .2% tri-kresol used as preservative. Cultures made—no growth.

Guinea-pig injected.

Oct. 12th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 13th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 14th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 15th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Oct. 16th.—1 cc. emulsion injected into peritoneal cavity—no reaction.

Pig in good condition, eats well.

Used for Wassermann complement satisfactorily. Autopsy.

Old infarcts of liver, old endocarditis, otherwise normal.

Following the guinea-pig experiment, I administered to myself in the anterior as-

pect of the thighs, six doses of from 3 to 6 cc. of the testicle emulsion. The only untoward effect was a slight swelling and redness of the skin following two of the injections of a full dose of the emulsion, and slight lameness—traumatic—for a day or two. There was no rise of temperature.

I subsequently employed the testicle emulsion quite freely in my clinical work, administering in all probably 100 doses, varying from 1 to 6 cc. to ten subjects. The cases were all pseudo-impotents and sexual neurasthenics, with the exception of one case, that of an elderly woman afflicted with senile pruritus.

From the apparent results of the treatment I concluded that the action of the emulsion was distinctly tonic. The male patients all stated that their condition had improved. To outward appearances the subjects in the main appeared better, color especially being improved. Several of the patients stated that they had a greatly increased appetite.

As to the possible psychic result, it could have been incidental only to the novelty of the treatment. None of the patients knew what he was taking. The case of senile pruritus was not improved, nor was any effect whatever noticeable. Some of the emulsions used in my experiments were more than eight weeks old when used. The spleen, liver

and pancreas used in preparing the emulsions were taken from a male subject of 25 years of age, dead twelve hours of cocaine poisoning. No effect of such amount of the drug as may have been contained in the tissue was noted. That narcotic poisoning does not destroy organ-cell vitality is proven by the fact that I successfully implanted a testis from the same subject. The testis has been in situ for twelve weeks and apparently is thriving.

The addition of tri-kresol to the emulsions may or may not have modified the results. With improved technique of preparation and use, it would be better to omit the preservative. If, however, it should be proved that the preservative is not detrimental, it would be better to employ it as a partial insurance against carelessness in manufacture, manipulation and administration.

CONCLUSIONS.

1. Properly prepared aseptic emulsions of organs from somatically dead human donors may be safely used for experimental-therapeutic purposes.
2. By virtue of their living cell content, emulsions or organs prepared without chemical preservatives, possibly may be a substitute for organ implantation in hormone therapy.
3. While emulsions free from preservative of any kind and kept properly refrigerated probably are more efficacious be-

cause of preservation of cell vitality in the organ material, therapeutic possibilities must be conceded to emulsions prepared with trikresol, and perhaps with other antiseptics.

4. Anaphylaxis, or other dangers, from the proteid content of the emulsions is not to be apprehended—at least from reasonable doses.

5. Organs from alien sources, i. e. from the lower animals, may safely be employed in emulsions used upon the human subject.

6. It may prove practicable in emergencies to furnish nourishment to the human body by the use of organ or other tissue emulsions from either the human or the lower animal subject.

7. Splenic emulsion, at least, and probably testicular emulsion, apparently is of therapeutic value. I should expect great results from thyroid emulsion.

8. Emulsions from organs from dead immunized human subjects may be of service in the "resistance therapy" of certain infectious diseases.

9. Even admitting the superiority of "extracts" in the treatment of disease, I believe that my emulsion work has opened up a promising field for the production of extracts from human organs, which logically should prove far more potent and efficient than similar extracts from corresponding organs of the lower animals.

10. Further experimentation by clinicians is desirable as tending to enlarge the scope of organotherapy.

32 N. State St., Chicago.