

experience in the injection of mercurial oil (gray oil) and other oil preparations. However, our warning is very definite to make the injection subcutaneously, and carefully to avoid getting the vaccine into a vein. After the needle has been introduced, the plunger of the syringe should be drawn out slightly, to be certain that the needle is not in a vein.

THE DYSENTERY LIPOVACCINE

In our previous publications we have indicated as our reason for considering that a dysentery lipovaccine would have a special advantage over a dysentery saline vaccine, that the slow absorption would reduce the reaction; and we gave some results of vaccination of animals and men with such a vaccine. As the series is now broken up, and a much more comprehensive series is under way, we wish to record the final results of the first series.

The vaccine contained 2,500 million each of Shiga, Flexner and "Y" types in 1 c.c., the strains that Gibson⁷ used in his vaccine being employed.

Three rabbits were injected with the vaccine, and showed the agglutinations given in Table 1.

TABLE 1.—AGGLUTINATIONS IN THE RABBIT

Rabbit	Dose	Agglutination		
		Shiga	Flexner	"Y"
16*	1 c.c.	1:100	1:800	1:400
17	1 c.c.	1:3,200	1:1,600	1:2,400
18	2 c.c.	1:100	1:400	1:1,600

*Rabbit 16 died two months after vaccination.

Two men were injected with the vaccine, and showed the agglutinations given in Table 2.

TABLE 2.—AGGLUTINATIONS IN MAN

R.†	Dose	Agglutination*		
		Shiga	Flexner	"Y"
St. J.	0.25 c.c.	1:200	1:200	1:37
St. J.	1 c.c.		None	

* The agglutinations of these men are reversed in the preliminary note.

† R passed from further observation.

Two and one-half months after vaccination, St. J.'s serum in dilution of 1:20 gave immediate cloudiness, and precipitation after two hours, with an extract of the Shiga type. His serum gave only a slight opalescence with extracts of the Flexner and "Y" types. Control serums remained clear.

Two and one-half months after vaccination, the serum of St. J. and of Rabbits 17 and 18 showed an opsonic index of from 0.26 to 0.82 for Shiga and Flexner, and an opsonic index of from 1.35 to 1.81 for "Y." In studying the smears made for the opsonic index, it was noted that there was marked bacteriolysis in all smears containing serum from the vaccinated animals and man. This may explain the low opsonic indexes; and this point is being studied in the new series.

Two and one-half months after vaccination, the serum of Rabbit 17 gave partial fixation of complement with all three types of the dysentery bacillus; the serum of Rabbit 18 and of St. J. showed no fixation of complement.

Two and one-half months after vaccination, Rabbit 18 received a dose of 2,700 million *B. dysenteriae* Shiga L intraperitoneally. The rabbit died during the night, apparently in about the same length of time as did the controls. The toxicity of this culture is such that 1,000 million intraperitoneally kill a rabbit in thirty-six hours.

7. Gibson, H. G.: A New Method of Preparation of a Vaccine against Bacillary Dysentery, Jour. Royal Army Med. Corps, 1917, 28, 615.

For the new series of animals and men we have used a vaccine containing 3,000 million Shiga, 3,200 million "Y," and 2,200 million Flexner per cubic centimeter, using the strains that Gibson⁷ used in his vaccine. Guinea-pigs stand up to 6 c.c. of this vaccine without ill effects; and we have vaccinated a series of men with 1 c.c. of this vaccine with no more local or general reaction than we get from a single dose of the regular triple typhoid vaccine in saline.

CONCLUSIONS

We find that the lipovaccines can be made on a large scale by growing the bacteria in Kolle flasks; taking off the growth with a vacuum scraper; freezing and drying in vacuo, and emulsifying in lanolin and oil by grinding in a ball mill, using glass bottles and steel balls.

The oils can be sterilized by steam at 15 pounds for fifteen minutes; by heating to 90 C. for ten hours on a water bath, or by mixing with potassium iodid.

We find that we can give men a dose of 3,000 million Shiga, 3,200 million "Y," and 2,200 million Flexner type of the dysentery bacillus in oil without marked local or general reaction. We find production of agglutinins, precipitins and bacteriolysins in the blood of vaccinated animals and men, and there is some evidence of complement fixation.

THE INFLUENCE OF FORCED DIURESIS IN EXPERIMENTAL POISONING WITH DIPHTHERIA TOXIN*

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This records an effort to apply the principle of forced diuresis or histolavage to the treatment of experimental poisoning with diphtheria toxin. As certain of the bacterial poisons are known to be capable of excretion in considerable amounts by way of the urine, a great acceleration of diuresis might appear to be a more rational procedure in the case of certain infections than in the case of poisoning with heavy metals. Diphtheria toxin was selected because it is sufficiently stable to permit of standardization. The work is reported for the sake of completeness along with that on glaucoma, mercuric chlorid poisoning, etc., since it serves to amplify our knowledge of what may or may not be accomplished by salt and sugar diuresis in general.¹

TECHNIC

The same general plan was followed as in the mercuric chlorid work.² The diphtheria toxin was a stable product 2 years old. The fatal dose was determined intravenously, but not with the same degree of precision as in the case of the mercuric chlorid, owing to the varying resistances found in the different animals. We found that 0.021 c.c. of the toxin per kilogram of body weight killed four out of five dogs in from three and one half to six days. One part of the toxin in 100 parts of 0.8 per cent. sodium chlorid solution was

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1. A fifth detailed report covering phases of work outlined in a preliminary communication (Woodyatt, R. T.; Sansum, W. D., and Wilder, R. M.: Prolonged and Accurately Timed Intravenous Injections of Sugar, THE JOURNAL A. M. A., Dec. 11, 1915, p. 2067).

2. Sansum, W. D.: The Principles of Treatment in Mercuric Chlorid Poisoning, THE JOURNAL A. M. A., March 23, 1918, p. 824.

administered intravenously in each case as a single dose. When diuretic treatment was to follow, the toxin was administered with the first few cubic centimeters of the diuretic solution. Three diuretic solutions were used: (1) an alkaline hypertonic salt solution (sodium chlorid, 2.2 per cent., and sodium carbonate, 0.371 per cent.; (2) an 18 per cent. glucose solution, and (3) an 18 per cent. glucose solution having the salt content of Ringer's solution (sodium chlorid, 0.7 per cent., potassium chlorid, 0.03 per cent. and calcium chlorid, 0.025 per cent.)

The diuretic solutions were administered as in the experiments described in previous publications. In the first series of four experiments we gave more than the predetermined fatal dose of diphtheria toxin in the hope of obtaining a decisive therapeutic result. These dogs received 0.030 c.c. of the diphtheria toxin per kilogram of body weight instead of the 0.021 c.c.

RESULTS OF EXPERIMENTS

No.	Wt. of Dog, Kg.	Total Dose of Diphtheria Toxin, C.c. per Kg.	Intravenous Therapy					Urine, C.c.	Duration of Life, Days
			Diuretic Solution	C.c. per Kg. Hour	Duration of Injection, Hrs.	Total Amt. Injected	Fluid Used to Preserve Water Balance		
1	11.25	0.021	3½
2	8.64	0.021	3½
3	12.28	0.021	6
4	15.11	0.021	6
5	14.28	0.021	14
6	11.82	0.030	4
7	10.91	0.030	5
8*	10.80	0.030	Alkaline salt solution	30	3	1,083	0	963	3
9*	5.11	0.030	Alkaline salt solution	30	4	628	915 c.c. water	827	5
10	20.00	0.021	Glucose, 18%	30	3	1,810	300 c.c. water	2,717	2
11	16.25	0.021	Glucose, 18%, in Ringer's solution	30	3	1,470	478 c.c. water	1,355	Lived
12	15.00	0.021	Glucose, 18%, in Ringer's solution	30	3	1,358	86 c.c. Ringer's	1,056	4
13	17.84	0.021	Glucose, 18%, in Ringer's solution	30	3	1,628	143 c.c. Ringer's	1,410	4
14	24.55	0.021	Glucose, 18%, in Ringer's solution	30	2	1,432	475 c.c. Ringer's	1,670	4
15	11.25	0.021	Glucose, 18%, in Ringer's solution	30	2	646	0	695	4
16	10.57	0.021	Glucose, 18%, in Ringer's solution	30	3	963	0	810	5

* Marked catharsis.

The two controls (Dogs 6 and 7) lived three and five days, respectively. The first treated dog (Dog 8), weighing 10.80 kg., received 30 c.c. of the alkaline salt solution per kilogram hour for three hours, a total of 1,083 c.c., and passed during that time 963 c.c. of urine. There was also a marked catharsis, which accounts for the urinary output being less than the fluid intake. This dog lived three days. The second treated animal (Dog 9), weighing 5.11 kg., received 30 c.c. of the same alkaline salt solution per kilogram hour for four hours, and also sufficient water from the second machine to prevent dehydration. During the four hours this dog received 1,543 c.c. of fluid, 628 c.c. of the alkaline salt solution and 915 c.c. of water, and passed 827 c.c. of urine and numerous watery stools. This dog lived five days.

We poisoned the remaining seven dogs in this series with the marginal fatal dose of diphtheria toxin, that is, 0.021 c.c. per kilogram. Dog 10, weighing 20 kg.,

received the 0.021 c.c. per kilogram with the first few cubic centimeters of an 18 per cent. glucose solution, which was given at the rate of 30 c.c. per kilogram per hour for three hours. During the three hours the dog received 1,810 c.c. of the glucose solution and 300 c.c. of water, and passed 2,717 c.c. of urine. This was the greatest diuresis of any in the series. The dog lived only two days, or less time than any other animal in the series. The treatment appeared to have done harm rather than good.

This phenomenon of shortening rather than prolonging life we had noted before in the mercuric chlorid series, and in searching for a possible cause considered the idea that it might be due to the wholesale washing out of urea, chlorids and other essential salts of the body. With the next group of six animals, we poisoned as before, and used an 18 per cent. glucose solution having the salt content of Ringer's solution, preserving the water balance by the addition of extra Ringer's solution when needed. Dog 11 made a complete recovery, but the next five animals (Dogs 12, 13, 14, 15 and 16) died in four, four, four, four and five days, respectively. We were inclined to believe that the dog which lived had an unusually high resistance for diphtheria toxin, since something similar had been observed in Control Dog 5, which lived fourteen days.

In these experiments, water was passed through dogs at the rate of 30 c.c. per kilogram of body weight per hour for three or four hours. The same procedure, if carried out in the case of a man weighing 70 kg., would imply the intravenous injection of 2,100 c.c. of fluid per hour for a total of 6,300, or 8,400 c.c. in three or four hours, nearly all of this passing promptly out by way of the kidneys and bowel.

CONCLUSIONS

The intravenous injection of an alkaline hypertonic salt solution, an 18 per cent. glucose solution or an 18 per cent. solution of glucose in Ringer's solution failed to prolong the life of dogs poisoned with diphtheria toxin even when treatment was begun at the most favorable time, that is, simultaneously with the administration of the poison. These negative results discourage attempts to apply an identical procedure in clinical cases of diphtheria.

Mammary Cancer in Infants.—Dr. D. Z. Blanc reported at a recent meeting of the Spanish Gynecologic Society that in the last year he had encountered two cases of cancer of the mamma in young infants. One was a male child. The mamma had begun to enlarge soon after birth and at the age of 6 months the epithelioma had invaded the entire mamma and the glands in the axilla, but there was no ulceration and the growth was not adherent to the pectoralis muscle. Blanc excised the mamma, the pectoralis and the contents of the axilla. Three months later the child died from recurring hemoptysis. In the other case the cancer developed in the same way soon after birth and in a few months spread to the axilla and into the hypochondrium. It was inoperable when he first saw the child. Blanc stated that hemorrhage from the lungs, probably of cancerous origin, is not an uncommon complication after removal of mammary cancers in adults. Injecting a stain under pressure into the lymphatics of the mamma to ascertain the area of probable diffusion, he found the entire pleura colored by the stain, both the parietal and the diaphragmatic pleura. His communication is reproduced in the *Revista de Medicina y Cirugia Practicas*, 1917, **41**, 216, with the hypothesis he presents to explain these cancers in the new-born.