acetylcholine. The basis of these effects, and their significance has been discussed.

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Prevention and Modification of Measles with Concentrated Pooled Ascites Fluid and with Its Globulin Fraction.*

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Various types of antibodies have been demonstrated in ascites fluid, but the presence of measles-protecting substances has not been reported. Since measles-protecting substances are found in the blood serum of most urban dwelling adults, it was thought of interest to test for their presence in a number of ascites fluids. Should these antibodies be present, the large amount of ascites fluid available in hospitals could provide an additional source of material for measles prophylaxis.

The ascites fluid was obtained from Wassermann negative individuals suffering from portal cirrhosis or cardio-vascular-renal disease. After Wassermann, Kline and sterility tests were found negative, a pool was made of aliquot parts of 9 fluids. Since less protein is present in ascites fluid than in serum it was realized that this fluid would have to be concentrated to provide a dose small enough to be practicable for intramuscular injection. The ascites fluid pool was divided into 3 parts. One portion was concentrated in sterile cellophane sausage casings by the corn syrup technic previously described,[1] another portion by the air technic,[2] and the globulin fraction was prepared by 50% ammonium sulphate precipitation.[3]

To obtain an amount of measles-protecting substances in concentrated ascites fluid equivalent to that in measles convalescent

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1 Thalhimer, W., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 230.

2 Thalhimer, W., PROC. SOC. EXP. BIOL. AND MED., 1938, **37**, 639.

3 Gibson, R. B., *J. Biol. Chem.*, 1906, **1**, 161.

serum or in pooled normal adult serum we calculated as follows: It has been found that about 4 volumes of pooled normal adult serum are necessary to give the same degree of passive immunity to measles as one volume of measles convalescent serum. Measles antibodies are contained in the globulin fraction of serum,[4, 5] as is true of other antibodies. Assuming that the globulin in ascites fluid is just as potent for measles prophylaxis as that in normal adult serum there would have to be as much globulin present in 1 cc of concentrated ascites fluid as in 4 cc of normal serum. Since normal serum contains 2% to 2.5% globulin, the concentrated ascites fluid would have to contain 4 times that amount, or 8% to 10% globulin.

The amount of globulin in the pooled unconcentrated ascites fluid was found to be 0.9%. The portion of the pool processed by the corn syrup technic was concentrated 9½ times, and was found by analysis to contain 9% globulin. The portion processed by the air technic was concentrated 5½ times, and analysis showed 5½ % globulin.† The other part was concentrated by globulin fractionation to one-tenth its original volume. If the separation of albumin and globulin had been complete this should have contained 9% globulin. However, analysis showed 7.2% globulin, a concentration of only 8 times or 20% loss of globulin, and, also, 1.4% albumin (Table I).

Since there is no laboratory method for determining the presence or amount of measles-protecting substances, we used a principle

TABLE I.

Ascites Fluid (Pool II), Concentrated by Two Cellophane Bag Methods and by Globulin Fractionation. Chemical Analyses and Assay of Diphtheria Antitoxin.

	Unconcentrated	Conc. by air method (5.5 times)	Conc. by corn syrup method (9.5 times)	Globulin fraction (Conc. 10 times)
Total Protein	2.4%	14. % (13.2%)†	25% (22.8%)†	8.6%
Albumin	1.5%	8.5% (8.25%)†	16% (14.25%)†	1.4%
Globulin*	0.9%	5.5% (4.95%)†	9% (8.55%)†	7.2% (9%)†
No. M.L.D.'s of Diph. Toxin neutralized by antitoxin in 1 cc	6	30-34 (36.6)‡	50-60 (60)‡	45-50 (48)‡

* Figures obtained by difference, after determining total protein and albumin.

† Figures in parentheses show the percentage calculated from chemical analysis of the original pooled ascites fluid on the basis of concentration.

‡ Figures in parentheses show diphtheria antitoxin calculated on the basis of the globulin content in the original pooled ascites fluid and globulin content of each concentrate.

[4] Karelitz, S., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 793.

[5] Karelitz, S., *Am. J. Dis. Child.*, 1938, **55**, 768.

† Because of the smaller amount of globulin in this concentrate prepared by the air technic a double dose was used.

introduced by Karelitz[6] of following the fate of another antibody, diphtheria antitoxin, in the original material and in the final preparations. The diphtheria antitoxin in the concentrated ascites fluids and in the globulin fraction increased in amount corresponding to the degree of the concentration of the globulin. Whereas the amount of diphtheria antitoxin is not an index of the amount of measles-protecting substances present, nevertheless this study demonstrated that the diphtheria antitoxin was not lost in these 3 methods of concentration if globulin was not lost, and it was expected that the measles-protecting substances, if present, would not be lost either.

Table I shows one typical pool, the degree of concentration, the percentage of total protein, albumin and globulin, and the amount of diphtheria antitoxin in the original pool and in the 3 concentrates.

The protective power of the 3 concentrates and of convalescent measles serum (used as a control) was determined clinically by administering them intramuscularly to healthy, susceptible children in crowded tenement houses where the contact had been intimately exposed to a member of the family developing measles. Under conditions of exposure of this type, about 90% of susceptible children will contract measles if unprotected. The dosage of the serums or concentrates was 10 cc, or a volume containing approximately an equivalent amount of globulin,† for all children regardless of age. The preparations were administered to all contacts from 4 to 7 days after exposure, considering the day the rash appeared in the patient as the 4th day after exposure. The contacts were observed daily or every other day from the 10th to 25th day after exposure. Rectal temperatures were taken on each visit. In this manner, mild forms of the modified disease, which might be overlooked, were detected, and the preparations were put to the severest test.

There were 23 children in the control group receiving regular measles convalescent serum; 24, receiving the globulin fraction of ascites fluid; 11, ascites fluid concentrated by the corn syrup technic, and 10, ascites fluid concentrated by the air technic. The results are shown in Table II.

That these preparations have a considerable ability to prevent and modify measles in the concentrations and quantities used, is shown by the fact that in all children where protection was not obtained the disease occurred in modified form, and not a single case of unmodified measles developed. In this series, though small, the measles prophylactic value of the ascites fluid, concentrated by the corn syrup and air technics respectively, appeared to be as good as and

[6] Karelitz, S., Greenwald, C. K., and Klein, A. J., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1359.

TABLE II.

Results Obtained in Prevention and Modification of Measles with Concentrates of Ascites Fluid and Measles Convalescent Serum.

Measles Convalescent Serum Pool M-23 Dose 10 cc			Ascites Fluid-Globulin Fraction Conc. 10 times Dose 10 cc			Ascites Fluid Conc. by corn syrup technic 9½ times Dose 10 cc			Ascites Fluid Conc. by air technic 5½ times Dose 20 cc		
Age	Day(*)	Result*	Age	Day(*)	Result*	Age	Day(*)	Result*	Age	Day(*)	Result*
8 mo	6	O	12 mo	6	O	13 mo	4	O	2 yr	4	O
16 "	3	O	15 "	5	O	18 "	6	A	2 "	5	O
16 "	5, 4, 3	A	16 "	7	B	22 "	7	B	4 "	5	O
17 "	4	A	18 "	5	B	2 yr	5	O	4 "	5	O
18 "	5	O	2 yr	6	A	2 "	5	A	5 "	5	O
20 "	4	O	2 "	6	B	3 "	5	O	5 "	7	B
22 "	7	B	3 "	3	O	3 "	7	O	6 "	3	O
2 yr	3	O	3 "	4	A	4 "	5	B	6 "	5	O
2 "	5	A	3 "	5	A	4 "	7	C	7 "	5	C
2 "	5	O	4 "	4	B	6 "	7	O	12 "	5	O
2 "	6	O	4 "	4	B	11 "	5	O			
3 "	4	A	4 "	5	C						
3 "	5	B	4 "	6	O						
3 "	6	O	4 "	6	B						
3 "	6	O	5 "	3	O						
4 "	5	O	5 "	5	O						
4 "	6	B	5 "	6	C						
5 "	4	A	6 "	5	C						
5 "	5	C	6 "	7	A						
5 "	5	B	6 "	7	O						
5 "	6	O	7 "	6	O						
7 "	7	O	8 "	4	O						
11 "	8	B	9 "	6, 5	B						
			12 "	8	B						
Results:		%			%			%			%
O	12	(52.2)	O	9	(37.5)	O	6	(54.5)	O	8	(80)
A	5	(21.7)	A	4	(16.6)	A	2	(18.2)			
B	5	(21.7)	B	8	(33.3)	B	2	(18.2)	B	1	(10)
C	1	(4.4)	C	3	(12.6)	C	1	(9.1)	C	1	(10)
	23			24			11			10	

* O—No disease developed. A—Extremely mild, barely recognizable modified measles. B—Mild, modified measles. C—Modified measles, definitely less severe than unmodified measles.

(*) Day of exposure on which the contact received the preparation.

better than that of the measles convalescent serum, while the globulin fraction in the concentration used was about three-fourths as efficient (Table II). The efficiency of these concentrates was proportional to their globulin content, the best results being obtained with the ascites fluid concentrated by the air technic, which contained 1.1 g of globulin in the 20 cc dose used. The next best results were obtained with the ascites fluid concentrated by the corn syrup technic, which contained 0.9 g of globulin in the 10 cc used. The least favorable results were obtained with the globulin fraction which contained 0.72 g per 10 cc. By increasing the amount or concentration of the globulin fraction results quite comparable to those obtained with measles convalescent serum and the ascites fluid concentrates should be obtained.

No local or general reactions occurred following the intramuscular injection of 10 cc of convalescent measles serum. Injection of the other solutions produced slight transitory local pain and stiffness in a small number of the children, but the temperature was seldom elevated above 100°. The injections of 20 cc amounts produced more local discomfort than the 10 cc doses.

In hospitals and private practice we have found that regular measles convalescent serum gives a higher percentage of protection than was obtained in this investigation. This is what one would expect where the exposure of contacts is less intimate and less prolonged, and the hygienic surroundings are better, and is in accord with the reported observations of others.[7, 8]

Summary. Measles-protecting substances have been found in pooled ascites fluid and its globulin fraction in sufficient quantities to be of practical value. The efficiency in measles prophylaxis of 2 concentrates of pooled ascites fluid and of a globulin fraction was found proportional to the globulin content of each preparation.

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[7] Park, W. H., and Freeman, R. G., Jr., *J. A. M. A.*, 1926, **87**, 556.

[8] Karelitz, S., and Schick, B., *J. A. M. A.*, 1935, **104**, 991.