POOLED BLOOD PLASMA TRANSFUSIONS IN THE TREATMENT OF LEPROSY *

By

G. H. FAGET

Senior Surgeon, United States Public Health Service (National Leprosarium), Carville, Louisiana

and

R. C. POGGE

Assistant Surgeon (R), United States Public Health Service (National Leprosarium), Carville, Louisiana

Serum treatment of leprosy is not new. As long ago as 1895 the use of the serum of animals previously inoculated with leprous blood was reported upon favorably in the treatment of leprosy by Carrasquilla of Colombia. His compatriot, Olaya Laverde, in 1897 inoculated animals with extracts of leproma rich in Hansen bacilli and used their sera in the treatment of leprosy. More recently Reenstierna claimed favorable results from the serum of sheep inoculated with cultures of both the Reenstierna and the Kedrowsky strain of acid-fast organisms recovered from leprosy patients. Finally Chala and Restrepo, of the Federico Lleras Acosta Institute of Colombia, revived the serotherapy of leprosy. Using various cultures of acid-fast organisms, including the strains of Lleras, Duval, Kedrowsky, and the No. 304 of the National Institute of Health, Chala and Restrepo inoculated sheep and goats. They report encouragingly upon this supposedly specific serotherapy of leprosy. However, the favorable results obtained by the originators of the various so-called specific serotherapies have not been generally confirmed by others.

As yet the use of normal human serum or plasma has not been given a fair trial in the treatment of leprosy. Blood transfusions have been employed on a small scale without definite beneficial results. Plasmotherapy in its various forms has been greatly stimulated by the present World War. Large supplies of human plasma have been made available not only for the armed forces but for civilian defense. Because pooled plasma is being so extensively used at present, it was thought timely to give it a fair trial in the treatment of leprosy.

The clinical indications for plasma transfusions are many. According to Strumia and McGraw, plasma is useful in shock, burns, hypoproteinemia, cerebral edema, hemorrhagic diseases, and infections.

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We are interested here only in the last indication. The therapeutic action of plasma against infection depends upon the specific and nonspecific antibodies which it contains.

There are three forms of therapeutic blood plasma: liquid plasma (which should be preserved in a refrigerator at 4°C. but can be kept at room temperature for some time), frozen plasma, and dried plasma. It is now known that the labile components of plasma, including the antibodies, complement, and prothrombin, are influenced by the method of preparation and preservation. Liquid plasma conserves a fair quantity of labile antibodies for a relatively short period of time. Frozen plasma preserves practically all of the labile elements, including prothrombin, so that on thawing it should have all the therapeutic value of freshly prepared plasma. Properly prepared and regenerated dried plasma loses only a portion of its antigens, prothrombin, and complement.

Since most adults seem to possess a relative immunity to leprosy, it was thought possible that some specific antibodies against the disease might be contained in their blood. These antibodies if preserved in the pooled plasma might prove effective against leprosy. For this reason attempts were made to obtain a supply of frozen or dried blood plasma. Unfortunately we were able to procure only liquid plasma. Although it was considered that this product had probably lost some of its specific elements and was not as suitable for our purpose as the frozen or desiccated form, its trial in leprosy was deemed justified.

Even if its antibody content was small, it might possess nonspecific qualities which could react favorably upon the complications of the disease. Furthermore, it might stimulate the patient's general bodily defensive mechanism. It has been observed that the majority of patients at the National Leprosarium are more or less anemic. The average red blood cell count of 100 consecutive patients on admission was 3,950,000 with 80 per cent hemoglobin. It is also noted that hypoproteinemia is frequent in leprosy, and that a reversal of the albumin-globin ratio is the rule. Nephritis and nephrosis are common complications in advanced stages of the disease. Destruction of tissue is extensive, and the erythrocyte sedimentation test is found to be even more rapid than in tuberculosis. Therefore, if no specific action resulted, it was thought that some and possibly all of the above conditions might be favorably influenced by frequent transfusions of pooled blood plasma.

Certain regulations and standards have been prescribed by the National Institute of Health for the proper preparation and preservation of pooled blood plasma. We were able to procure an adequate supply of such properly prepared liquid blood plasma from Dr. J. W. Davenport, of the Southern Baptist Hospital, in New Orleans. This

pooled plasma was prepared so that each lot was made from the blood of at least eight donors, and it was expected that the plasma would contain some of the specific and non-specific antibodies of each of these donors. Because of pooling, its administration was simplified, eliminating the necessity of preliminary typing and compatibility tests. Freedom from reaction was assured, and this made possible its administration in large doses and concentrated form.

The group of patients treated were not selected but volunteered for this treatment after its possible beneficial effects were explained to them. Among the twelve patients who consented to undertake the treatment, six of them were unfortunately far advanced and practically hopeless cases. In only three of the remainder was the disease in a sufficiently early stage for reasonable expectation of benefit from any type of treatment.

Clinically the disease was classified as of the mixed type in 7 patients, lepromatous in 4, and neural in 1. This is shown in the third column of the table by (LN), (L), and (N), with the degree of involvement indicated by the numbers 1, 2, and 3, in accordance with the classification adopted by the last international conference on leprosy. Further details of the condition of the patient before and after treatment are also included in the table.

Summary and Conclusions

Of the twelve cases there was possible improvement in two (1406 and 1441). Definite unfavorable progress in leprosy was noted in five cases (971, 1289, 1521, 1525, and 1550). No demonstrable effect was noted in the leprosy of the remaining six cases (979, 1037, 1117, 1160, 1209, and 1566). Disappointingly, two of the three cases in which the prognosis seemed most favorable reacted unsatisfactorily and the third was not definitely benefited by pooled plasma therapy.

In three cases a variation in the non-protein nitrogen of the blood was observed, showing in two cases (1117 and 1160) a decrease in nitrogen retention and in one (971) a rise.

Of three cases with hypoproteinemia (971, 1117, and 1037), there occurred an increase in total serum protein in two without any appreciable change in the albumin-globin ratio, and the third patient died before the blood chemistry could be repeated.

Red blood cell counts dropped sharply in seven cases (971, 979, 1160, 1209, 1441, 1550, and 1566) out of ten observed carefully, while in the other three (1117, 1289, and 1406) there was an increase.

The writers therefore believe that at present there is no evidence to indicate that non-specific liquid blood plasma has any value in the

Observations made on patients treated with pooled Blood Plasma

Reg. No.	Age Sex Race	Type of disease	Duration in years	Hospitalization in years	Complications and intercurrent diseases	PREVIOUS LABORATORY FINDINGS: Smears Skin	Smears Nasal	Red blood cells million/cm	Hemoglobin per cent	White blood count no/cm	Differential count per cent	Urinalysis	Blood chemistry no/100cc	Sedimentation rate mm/hr (Cutler)	Previous treatment: Type	Previous treatment: Result	Plasma transfusion treatment: Number Amt. and period 15c to 650 cc.	Reactions	Results	SUBSEQUENT LABORATORY FINDINGS: Smears Skin	Smears Nasal	Red blood cells million/cm	Hemoglobin per cent	White blood cells no/cm	Differential count per cent	Urinalysis	Blood chemistry no/100cc	Sedimentation rate mm/hr (Cutler)	Remarks
971	44 M W	L_4N_1	13	5	Leprous laryngitis, nephritis, anemia	+	+	2.38	48	3,800	Stab. 8 Seg. 72 Lym. 18 Mon. 2	Albumin, casts, red blood cells	NPN 42 mgm Protein 4.25gm Albumin 2gm Globulin 2.25gm A/G ratio 0.8	36	Chaulmoogra oil, hydnocarpus esters, diphtheria toxoid	Gradually getting worse	12 doses total 3,000 cc. 1½ months	None	Worse	+	+	1.34	40	1,200	Stab. 2 Seg. 57 Lym. 43 Mon. 3	Albumin, casts	NPN 64.2mgm Protein 6gm Albumin 2gm Globulin 3.9gm A/G ratio 0.5	38	Emergency tracheotomy necessary two months after discontinuing treatment. Died of nephritis three months later.
979	54 M W	L_4N_3	9½	8	Leprous ulcerations and gangrene, syphilis	+	*	4.10	80	11,300	Stab. 6 Seg. 45 Lym. 40 Mon. 6 Eos. 3	Negative	NPN 50mgm Protein 8.5gm Albumin 3.4gm Globulin 5.1gm A/G ratio 0.6	30	Chaulmoogra oil, hydnocarpus esters, neosalvarsan, Bismo-Cymol, diphtheria toxoid, sulfathiazole	Growing worse	9 doses total 2,925 cc. 2 months	None	No change	+	*	3.33	74	3,350	Stab. 4 Seg. 57 Lym. 39 Mon. 4	Negative	Protein 7gm Albumin 2.9gm Globulin 4.1gm A/G ratio 0.7	30	Continues to develop small gangrenous patches and petechia. No favorable change in skin lesions.
1117	25 F W	L_2N_1	13	10	Leprous laryngitis, leprous keratitis, nephritis	+	+	3.66	74	7,150	Stab 6 Seg. 64 Lym. 22 Mon. 8	Albumin, casts, red blood cells	NPN 56.6 mgm Protein 4.6gm Albumin 1.9gm Globulin 2.7gm A/G ratio 0.7	30	Chaulmoogra oil, diphtheria toxoid, sulfathiazole	Gradually getting worse.	58 doses total 14,750 cc. 5½ months	None	No change	+	+	3.94	78	7,450	Stab. 10 Seg. 45 Lym. 30 Mon. 12 Eos. 3	Casts, red blood cells	NPN 31.3mgm Protein 5.8gm Albumin 2.2gm Globulin 3.6gm A/G ratio 0.6	26	Some improvement in hypoproteinemia. Otherwise condition is stationary.
1037	64 F W	L_4N	10	7	Leprous ulcerations, malaria bronchitis, arteriosclerosis, hypertension, nephritis	+	+	3.59	50	5,700	Stab. 15 Seg. 66 Lym. 17 Mon. 2	Albumin, casts, pus cells, red blood cells	NPN 50mgm Protein 4.25gm Albumin 2.9gm Globulin 1.35gm A/G ratio 2.2	30	Chaulmoogra oil, diphtheria toxoid, Fowler's solution, strychnine	Worse, prognosis poor	28 doses total 8,950 cc. 5 months	None	No change	*	*	*	*	*	*	*	*	*	Death due to cerebral hemorrhage during course of treatment five days after last plasma transfusion. Highest blood pressure 190/95.
1160	27 M W	$L\ N_3$	11	9	nephritis, anemia	+	+	2.81	50	17,900	Stab. 10 Seg. 66 Lym. 16 Mon. 4 Eos. 4	Albumin, casts, red blood cells	NPN 60 mgm Protein 6.2gm Albumin 2.5gm Globulin 3.7gm A/G ratio 0.7	34	Chaulmoogra oil, diphtheria toxoid, Fowler's solution, cod liver oil	Disease worse, prognosis poor	30 doses total 9,650 cc. 5 months	None	No change	+	*	1.92	25	36,950	Myel. 2 Juv. 3 Stab. 23 Seg. 67 Lym. 7 Mon. 1	Albumin, casts	NPN 56.2mgm	*	An alveolar abscess developed during course of plasmotherapy which progressed to gangrenous stomatitis and septicemia. Patient died of same one month following plasmotherapy.
1209	60 M W	L_4N_3	7	5	Leprous neuritis, ulcerations and gangrene, pulmonary tuberculosis (minimal)	+	*	3.37	88	9,800	Stab. 8 Seg. 57 Lym. 34 Mon. 6	Negative except few hyaline casts	*	25	Chaulmoogra oil, hydnocarpus esters, diphtheria toxoid	Worse, prognosis poor	7 doses total 2,650 cc. 3 months	Icterus, chills and fever last two transfusions	No change	+	*	3.05	80	6,600	Stab. 31 Seg. 59 Lym. 8 Baso. 2	Casts, bile, red blood cells	*	*	Cirrhosis of liver developed with jaundice, ascites, and emaciation during course of therapy, producing death 3 months after last transfusion.
1289	28 M W	L_4	6	4	Secondary anemia	+	+	3.25	80	5,300	Stab. 9 Seg. 44 Lym. 39 Mon. 2 Eos. 6	Negative	*	24	Chaulmoogra oil, diphtheria toxoid	Worse	28 doses total 7,375 cc. 3½ months	None	Worse	+	+	3.81	74	5,800	Stab. 5 Seg. 60 Lym. 32 Mon. 2 Eos. 1	Negative	*	27	New lepromatous nodules developed on face and legs. Some former nodules grew larger.
1406	25 F C	L_4	3	1	Nephritis anemia	+	+	3.63	65	6,650	Stab. 12 Seg. 62 Lym. 17 Mon. 4 Eos. 3 Baso. 2	Albumin, casts, pus cells, red blood cells	*	23	Chaulmoogra oil, diphtheria toxoid	Worse	24 doses total 6,000 cc. 3 months	Vertigo after one transfusion	Improved	+	*	5.15	88	7,250	Stab. 5 Seg. 53 Lym. 25 Mon. 6 Eos. 11	Negative	*	22	Improved, many nodules on face smaller, some completely absorbed. Nodules on limbs, no change. Patient's general condition improved; anxious to continue treatment.
1441	29 F C	L_4N	6	1½	Leprous laryngitis, leprous rhinitis	+	+	4.24	90	7,750	Stab. 5 Seg. 50 Lym. 26 Mon. 12 Eos. 6 Baso. 1	Pus cells, red blood cells	*	24	Chaulmoogra oil, diphtheria toxoid	Worse, especially laryngitis	12 doses total 2,750 cc. 1½ months	None	Slightly improved	+	+	3.89	82	6,200	Stab. 7 Seg. 64 Lym. 27 Mon. 2	Red blood cells	*	25	Subjective improvement in visual acuity. Questionable improvement in lepromatous lesions. Emergency tracheotomy to save life, 6 weeks after discontinuing plasma.
1525	18 M Y	N_3	7/12	1/12	None	+	—	*	*	*	*	Negative	*	7	None	New case	2 doses total 500 cc. two weeks	Severe leprous reaction each transfusion	Worse	+	*	3.59	85	5,300	Stab. 6 Seg. 60 Lym. 33 Eos. 1	Negative	*	14	Severe leprous reaction with chills and fever and erythema multiforme eruption of face, neck, and left arm following each transfusion. Afterwards a facial paralysis developed.
1550	20 M W	L_4	10/12	1/52	None	+	*	4.30	82	10,400	Stab. 6 Seg. 66 Lym. 24 Mon. 4	Negative	*	23	None	New case	15 doses total 3,000 cc. 1½ months	None	Worse	+	*	3.46	72	7,800	Stab. 13 Seg. 55 Lym. 31 Mon. 1	Negative	*	*	Increase in number of lepromatous nodules and in superficial ulcerations.
1566	28 M C	L_4	1½	2/12	Secondary anemia	+	+	3.48	62	6,600	Stab. 14 Seg. 54 Lym. 18 Mon. 4 Eos. 8 Baso. 2	Negative	*	30	None	New case	28 doses total 7,840 cc. 3½ months	None	Worse	+	*	3.39	66	9,300	Stab. 25 Seg. 53 Lym. 17 Mon. 5	Trace of albumin	*	25	No change in lepromatous lesions but ulcers developed on lower extremities. Patient absconded after last transfusion and returned to hospital in 3 months in worse condition.

* not done.

treatment of leprosy. Whether frozen blood plasma with its higher content of antibodies in a specially selected group of early cases would be more effective therapeutically is problematic.

Bibliography

Chala, H. J. I. and Restrepo, F. L., Tratamiento biologio en la lepra. Suero-terapia-antileprosa. Revista Colombiana de Leprologia. **3** (April-September 1941) 1-2.

Davenport Jr., J. W. Pioneering in plasma service. The Mod. Hosp. **60** (January 1943) 1.

Garcia, M. P., Rapport fait pas le Docteur Pablo Garcia Madina a la Semaine Medicale de Paris sur la Troisieme Communication du Docteur Carrasquilla. Semaine Medicale. **44** (September 2, 1896).

Reenstierna, J. A fourth orientation on the therapeutic value of an antileprosy serum. Internat. J. of Leprosy. **6** (January-March 1938) 1.

Reenstierna, J. Further therapeutic tests with an antileprosy serum. Acta Med. Scandinav. Supplementum CXVIII (1941).

Strumia, M. M. and McGraw, J. J. Blood plasma—its place in the practice of medicine, with special preference to the problem of preservation. J. A. M. A. **118** (February 7, 1942) 6.