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Different Fractions of Plasma Proteins in Some Infectious Diseases. (22983)

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Changes in plasma protein patterns usually manifest themselves by increase or decrease in concentrations of normal components or by appearance of protein fractions not seen under normal conditions. Different fractions of plasma proteins have been determined in different diseased conditions(1-6) but such studies in patients suffering from acute infectious diseases like cholera, small pox, tetanus and meningitis have not been published. The present communication deals with such studies in patients suffering from cholera, tetanus, small pox and meningitis by paper electrophoresis. Similar studies were also carried out in normal Indians for comparison.

Methods. Blood samples were collected in vials, containing crystals of potassium oxalate, from the anticubital vein as soon as patients suffering from small pox, tetanus and meningitis were admitted to the hospital. In patients suffering from cholera, blood samples were withdrawn when dehydration of the body was controlled by transfusion of saline and patients had normal urination. Normal subjects were students of our department of physiology. Total nitrogen in .1 cc plasma and nonprotein N in tungstic acid blood filtrate equivalent to 0.5 cc plasma were determined by the micro-Kjeldahl method. By multiplying the difference between the total N and nonprotein N with 6.25, total protein value of blood plasma was obtained. Fibrinogen was determined in 1 cc plasma by isolation as fibrin according to the method of Cullen and Van Slyke(7) and determination of N in fibrin by the micro-Kjeldahl method. 1 cc plasma was diluted 3 times with barbiturate-barbituric acid buffer of pH 8.6 and ionic concentration .05. .02 cc of the dilute plasma was applied to paper strip and electrophoretic separation was carried out for 12 hours by using L.K.B. paper electrophoresis apparatus with current of 6 mA and 300 volts. The filter paper strips were dried at 100°C, immersed in .1% bromophenol blue in absolute ethanol saturated with mercuric chloride for 30 minutes, washed in .5% acetic acid, dried, optical density curves of the different colored zones plotted using Photovolt Photoelectric Densitometer Model 425 on graph paper, and areas of component sections of graph were measured by cutting out the curves and weighing in micro balance. Total area of plotted curve was equivalent to total plasma protein content of sample used for electrophoresis, determined by the micro-Kjeldahl method. Weight of component sections of curves was proportional to area and protein value of each component was calculated from total protein value. As γ-globulin and fibrinogen zones in the electrophorogram were almost inseparable, the former was determined by deducting the sum total of albumin, α-globulin, β-globulin and fibrinogen values from the total protein value. The results are given in Table I.

TABLE I. Different Fractions of Plasma Proteins (%).

Subjects	Total protein	Albumin	α-globulin	β-globulin	γ-globulin	Fibrinogen
Normal (22)	8.22 ± .1*	4.64 ± .11	1.11 ± .06	.77 ± .05	1.39 ± .05	.31 ± .02
Cholera (16)	6.39 ± .10	2.26 ± .08	.84 ± .05	1.37 ± .08	1.47 ± .09	.45 ± .02
				(B_1) .79 ± .07		
				(B_2) .71 ± .04		
t	12	17.1	3.5	6.3	.8†	6.1
Small pox (10)	6.33 ± .06	2.40 ± .14	1.02 ± .08	.89 ± .08	1.78 ± .12	.44 ± .02
					(γ_1) 1.13 ± .11	
					(γ_2) .65 ± .05	
t	5.9	12.5	.89†	1.2	3.5	4.6
Tetanus (11)	8.02 ± .22	2.92 ± .22	1.52 ± .08	1.16 ± .08	1.90 ± .14	.52 ± .04
t	.79†	6.9	4.2	4.2	3.4	4.6
Meningitis (10)	6.83 ± .29	2.28 ± .15	1.22 ± .09	.95 ± .09	1.59 ± .22	.79 ± .05
t	4.5	12.3	1.1†	1.7†	.90†	8.4

* Stand. error. † All values of *t* except these values are significant.
Figures in parentheses indicate No. of subjects studied.

Results. Cholera: β-globulin was high and was differentiated into β_1 and β_2 fractions. Fibrinogen increased. Total protein, albumin and α-globulin diminished. γ-globulin did not change. *Small pox*: Total protein and albumin diminished. No change in α- and β-globulins. Fibrinogen and γ-globulin increased and the latter was differentiated into γ_1 and γ_2 fractions. *Tetanus*: The different fractions of plasma globulins and fibrinogen increased. Albumin was low. Total plasma proteins did not change. *Meningitis*: The different fractions of globulins increased but values were not statistically significant. Total protein and albumin were low. Fibrinogen was high.

Discussion. Cholera: Diminution in plasma proteins might be partly due to hydremia as a result of saline transfusion, as average packed cell volume was 35%. It might also be due to disintegration of plasma proteins, as non protein N values were very high varying between 80 and 120 mg/100 cc blood. There might be possibility of decreased synthesis of albumin and α-globulin. High level of β-globulin in cholera might be due to stability of this protein complex by some mechanism as suggested by Tayeau(8). Elevation of fibrinogen in cholera is very significant. This might be due to dysfunction of the liver. The lowered albumin content might also indicate liver dysfunction(9,10). Antibodies are mainly contained in the γ-globulin of plasma proteins(11). As cholera is a very acute infectious disease and the disease is not prolonged, antibodies cannot find time to accumulate. This might explain the normal value of γ-globulin in cholera.

Small pox: Hypoproteinemia might be due to decreased synthesis of plasma proteins or due to its increased demand for formation of tissue protoplasm, which is continuously destroyed during the course of the disease. Fibrinogen is significantly raised in small pox possibly due to dysfunction of the liver. The increase in γ-globulin suggests formation of antibodies during the disease possibly by proliferation of lymphoid tissue(12,13). Antibody activity is more pronounced in γ_1 than in γ_2 fraction. Concentration of γ_1-globulin is nearly twice that of γ_2-globulin.

Tetanus: α-globulin is raised in pathological processes involving tissue destruction(14). Increased α-globulin in tetanus might also be due to increased tissue destruction. β-globulin increase might be due to stability of this protein complex(8). γ-globulin increase indicates increased antibody formation and increase in fibrinogen might be due to liver dysfunction.

Meningitis: It appears that in meningitis, the liver functions in an abnormal way as a result of which albumin decreases and fibrinogen is increased. The low albumin might also be due to albuminuria. Normal globulin

suggests that antibody formation does not proceed with the disease.

Summary. Different fractions of plasma proteins were determined by paper electrophoresis in 16 patients suffering from cholera, in 11 cases of tetanus, 10 cases of meningitis, 10 cases of small pox and 22 normal subjects. Total protein was lower than normal in all diseases studied except tetanus. Albumin was lower and fibrinogen was higher in all diseases as compared to normal values. Of the globulins, cholera cases had low α, increased β and normal γ-globulins. β-globulin contained β_1 and β_2 fractions not seen in normal persons. In patients suffering from small pox α- and β-globulin fractions were normal but γ-globulin fraction which increased, contained γ_1- and γ_2-fractions. In patients suffering from meningitis and tetanus all the globulin fractions increased but in meningitis these increased values were not statistically significant. The implication of these changes has been discussed.

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Cortisone and Mortality in Mouse Typhoid. I. Effect of Hormone Dosage and Time of Injection.* (22984)

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The effect of cortisone on progress of bacterial infections remains a controversial issue. Some studies have indicated that this hormone lowers resistance(1,2). Other experiments have demonstrated that cortisone, in small quantities, will increase natural resistance to infection(3,4). This disagreement is of interest in regard to the *Salmonella* diseases, inasmuch as cortisone has been recommended as an adjunct in treatment(5). The following data summarize a study of the effects of cortisone on mortality of 4 strains of mice genetically differentiated for resistance to *Salmonella typhimurium*.

Materials and methods. Four inbred mouse strains from our Laboratory were used in this study: S, Z, K, and BALB/Gw, indicated as Ba. Each strain has been inbred by over 30 generations of brother-sister matings and, as a result, has become a distinct biotype with characteristic level of resistance to mouse typhoid. The wide range in resistance of these 4 strains may be seen in Table I. All mice were 5½-6½ months old. *Bacterial inocula-*

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