15 M protein. In addition to these similarities obtained by extraction methods and by trypsin treatment, extracts of glossy variants of the 2 Type 15 strains available for study did not contain the factor which formed a precipitate with human sera. This finding served to differentiate the unknown reactive factor from an R antigen, as R antigens, almost by definition, are extractable by usual methods from glossy strains, and react to form a precipitate with rabbit antisera prepared against R containing matt strains of the homologous type.

It was thus evident that the unknown protein factor extractable from Group A Type 15 matt strains of streptococci was not a T antigen and not an R antigen. Certain of its properties were similar to those of M antigens, but precipitin reactions between M containing extracts of Group A streptococci and sera of patients who have had infections even with homologous strains have never been obtained. Even were precipitin reactions between sera of patients convalescent from streptococcal infections and extracts of the infecting strains obtainable, it would be most improbable that a random population of 137 individuals would all have had infections with Type 15 streptococcus. Human infection with Group A, Type 15 streptococci is extremely uncommon.

Summary. A precipitation reaction between extracts of Group A, Type 15 streptococci and human serum has been described. The streptococcal factor bears some similarity to the M protein, but is almost certainly a separate substance, probably protein in nature. Like the M, T and R antigens it is present on the surface of the streptococcal cell. The reactive factor has been differentiated from T and R antigens. It is not yet known whether or not the bacterial factor is antigenic, nor is it known yet whether the reaction between this factor and human serum is of other than a happenstance nature.

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Effect of Histamine on F_{cells} Value in Splenectomized Dog.* (24809)

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The overall cell percentage venous cell percentage (F_{cells}Factor) is less than one in the splenectomized dog(1,2) as well as in man (3). The generally accepted explanation is that the blood in the small vessels and capillaries has a lower cell percentage than that in the large veins and arteries(1,4,5,6). Hence, the F_{cells} value is presumably influenced by the fraction of blood present in the minute vessels. Superficially at least, circulation through the small vessels and capillaries appears to be quite variable and subject to many influences (temperature, bleeding, infusions, psychic states, functional demands of the tissues and a variety of other neural and humoral stimuli). And yet, in the splenectomized dog, drastic changes in volume and composition of the blood appeared to have little effect upon the F_{cells} value(2). It was reported from this laboratory by Deyrup that in unanesthetized dogs subcutaneous injection of histamine causes prolonged reduction in blood pressure(7) and cardiac output(8), but

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no reduction in blood volume(7). In the splenectomized dogs included in Deyrup's series, plasma volume increased somewhat after histamine, whereas venous cell percentage remained essentially unchanged, indicating that the ratio, overall cell percentage/venous cell percentage, probably had decreased. This has now been demonstrated in the experiments described below which show that in the splenectomized dog histamine does bring about a marked reduction in F_{cells} value which almost doubles the calculated percent "extra plasma."

Materials and methods. The experiments were done on 10 healthy mongrel male dogs, splenectomized at least 1 month before experiments. The dogs were accustomed to lying quietly during measurements of blood volume. In 5 experiments (Group A), a polyethylene catheter was inserted into a branch of one femoral artery under local novocain anesthesia for continuous recording of blood pressure and heart rate on a Sanborn-Twin-viso recorder. Cell volume was determined with Cr^{51} and plasma volume with T-1824 as described previously(9). Injections of Cr^{51} and T-1824 were made 40 minutes before giving histamine diphosphate subcutaneously (3 mg of histamine base/kg body weight) and once again in each experiment at some point during the period of histamine hypotension. The times of the second Cr^{51} and T-1824 injections ranged from 46-89 minutes after giving histamine. Cr^{51} and T-1824 were injected into the femoral vein, but all blood samples were drawn from the indwelling arterial catheter. In addition to the Cr^{51} and T-1824 determinations, the hematocrit value and plasma protein concentration were measured on each sample. In 5 other experiments (Group B), the first T-1824 injection was omitted to minimize the effects of blood sampling and also to eliminate the residual dye in the blank sample for the post-histamine plasma volume measurement. In this group, initial plasma volume was calculated from initial cell volume by assuming the F_{cells}Factor of 0.87(2). Also, only one Cr^{51} injection was made at the start, post-histamine cell volume being calculated from initial cell volume by subtracting the counts removed in sampling. Dose of subcutaneous histamine given in this series ranged from 3.6-4.7 mg/kg. Time of the post-histamine T-1824 injections ranged from 30-110 minutes after giving histamine. Three of the Group B experiments were done under Nembutal anesthesia.

Results. Changes in blood pressure and heart rate were essentially the same as those described by Deyrup(7). Within 1-2 minutes following subcutaneous injection of histamine, the blood pressure fell from average control value of 143 to 30-60 mm Hg and was maintained at these low levels for several hours while heart rate increased from average control value of 102 beats/minute to about 200 beats/minute.

Data on cell and plasma volume before and after histamine are tabulated in Table I. Group A includes experiments on unanesthetized dogs in which cell and plasma volumes were directly determined before, as well as after histamine by repeating the injections of Cr^{51} and T-1824. In Group B, as stated above, volume changes were calculated from one Cr^{51} injection before giving histamine and one dye injection after giving histamine.

In Group A cell volume after histamine injection averaged 24 ml less than the control. The cells removed in blood samples averaged about 20 ml. Hence, the small decrease in cell volume is largely accounted for by sampling and appears to justify the calculations for Group B described above. It will be noted that plasma volume increased after histamine. This is reflected in the decrease in plasma protein concentration.

Changes in arterial cell percentage show no consistent trend in the experiments on unanesthetized dogs, but appear to increase in the dogs under Nembutal. This may be related to the changes in depth of anesthesia and possibly also to the volume of samples which is somewhat higher in Group A.

The important fact revealed by the results in Table I is the large drop in F_{cells}Factor after giving histamine. In the Group A experiments, where dose of histamine was 3 mg/kg body weight throughout, average post-histamine F_{cells} value is 0.79, as compared with the average control of 0.86 which falls

TABLE I. Observed Changes in Cell Volume, Plasma Volume, Arterial Hematocrit Value, Plasma Protein Concentration and F_{cells} Value in Splenectomized Dogs Given Histamine Subcutaneously.

Wt, kg	Hist., mg/kg		C.V., ml	P.V., ml	Het., %	P.P., g %	F_{cells}
			Group A				
12.5	3	Control	360	522	48.1	7.12	.848
		46′ post hist.	349	569	47.2	6.80	.805
11.0	3	Control	400	588	47.1	7.07	.860
		75′ post hist.	378	624	48.0	6.77	.786
17.7	3	Control	469	750	45.2	6.59	.852
		89′ post hist.	429	765	48.0	6.36	.747
11.6	3	Control	290	586	39.5	6.31	.838
		76′ post hist.	268	600	39.5	6.02	.782
11.0	3	Control	385	639	41.2	5.91	.912
		60′ post hist.	350	692	40.7	5.78	.826
			Group B				
6.6	4.0	Control	169	318	39.9		
		30′ post hist.	165	357	40.6		.778
13.0	4.2	Control	230	744	27.1		
		60′ post hist.	228	746	31.0		.755
† 5.8	3.6	Control	149	327	36.0		
		70′ post hist.	146	367	39.0		.731
† 12.0	4.7	Control	337	654	39.1		
		110′ post hist.	332	717	43.0		.735
† 10.8	3.5	Control	353	804	35.1		
		60′ post hist.	348	895	37.6		.744

* Control plasma volumes were calculated from control cell volumes and hematocrit, using F_{cells} of 0.87.

† Dogs under Nembutal anesthesia.

within the range of previously determined normal values with Cr^{51} and T-1824(9). In the 2 unanesthetized dogs in Group B receiving 4.0 and 4.2 mg/kg histamine, average F_{cells} value is 0.77. In the Nembutalized dogs given 3.5-4.7 mg/kg average F_{cells} value is 0.74.

Discussion. It is of interest to compare above results with calculations based on Deyrup's data(7). We include here 4 of her experiments on dogs splenectomized at least one month prior to histamine tests in which plasma volume change was observed ½ to 1½ hours after histamine injection. Although she did not measure cell volume directly, the initial cell volume can be calculated with considerable certainty from plasma volume and hematocrit values§ utilizing the F_{cells}Factor since we know that the latter lies close to 0.87 (2). From the initial cell volume, post-histamine cell volume can then be estimated rather closely by subtracting volume of cells removed in samples taken prior to histamine injection.

The F_{cells} values calculated from Deyrup's dogs 19-22 inclusive(7), are listed in Table II, together with post-histamine F_{cells} values

TABLE II. F_{cells} Values in Unanesthetized, Splenectomized Dogs after Histamine Injection.

Dog No.	F_{cells} after histamine
1	.805
2	.786
3	.747
4	.782
5	.826
6	.778
7	.755
19 D*	.781
20 D	.749
21 D	.797
22 D	.782
Avg	.781
Stand. dev.	.024

* D denotes dogs in Deyrup's series (1944). F_{cells} values for these dogs are calculated as described in text.

§ These hematocrit values are not listed in Deyrup's paper, but may be calculated from plasma volumes and total blood volumes given in her tables.

obtained in the present series of experiments. It is apparent that the calculations from Deyrup's experiments are in close agreement with the values obtained in the present experiments, and that all values listed in the Table fall below the range of normal values. The difference between average post-histamine F_{cells} value and average normal F_{cells} value, determined by Rawson, *et al.*(9) also utilizing Cr^{51} and T-1824, is highly significant. This is also shown by direct comparison of control and post-histamine F_{cells} values in individual dogs of Group A (Table I).

The term "extra plasma" refers to the percent of plasma left over when one calculates the plasma required to contain all the cells in the circulation at the concentration obtaining in the large vessels from which samples are drawn. In the normal unanesthetized splenectomized dog, extra plasma amounts to about 13% of the total blood volume(1,2). After injection of histamine, the proportion of "extra plasma" increases to 22% as given by the F_{cells} value. Since histamine causes widespread dilatation of the minute vessels(10), it may be inferred that the increase in percent "extra plasma" is the result of a larger proportion of the blood being present in the small vessels. However, it could also be a consequence of a decrease in cell percentage of the blood of the small vessels. Both factors may be operative, but the former seems the more likely explanation.

Summary. From ½ to 2 hours after subcutaneous injection of histamine (3.0-4.7 mg/kg) the average F_{cells}Factor of splenectomized dogs decreased to 0.78 from the control value of 0.87.

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A New Member of Hepatoencephalitis Group of Murine Viruses. (24810)

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Frequent occurrence of latent agents of infectious diseases in apparently healthy laboratory animals may be responsible for error in interpretation of isolation procedures. A number of transmissible agents have been procured within recent years by serial passage of supposedly "normal" mouse tissues. Some of these, namely the ascites-hepatitis agent isolated in mice in Mirick's laboratory(1) and the mouse ascitic agent recovered in mice at Walter Reed Army Inst. of Research(2), are associated principally with ascites and hepatosplenomegaly. In addition to these agents, mice may harbor latent viruses which produce massive macroscopic necrosis of liver and which on intracerebral inoculation into suckling or weanling mice may or may not induce fatal encephalitis. The latter group of agents is designated murine hepatoencephalitis group of viruses(3). The disturbing frequency with which members of this group of viruses were encountered in commercially procured mice in our laboratory in Japan in 1956 through 1958, in human hepatitis isolation studies prompts this report. It is the purpose of this paper to delineate murine hepatoencephalitis group of viruses and to add to it a new member.

Materials and methods. Viruses. Three