

1. Both complement and thrombin are non-specific. Complement obtained from one animal will react with the amboceptor and antigen of another species. Thrombin from various animals will clot fibrinogen irrespective of its source.

2. Both thrombin and complement, particularly the *mid-piece*, are associated with the globulin fraction of the serum proteins.

3. Prothrombin, thrombin, and complement are inactivated at 56°C., and the resulting serum or plasma becomes antithrombic and distinctly anticomplementary (the plasma more than the serum).

4. Serum or plasma treated with an emulsion of magnesium hydroxide becomes antithrombic (anti-clotting), and anticomplementary, with the effect more pronounced in the plasma than in the serum.

5. Heparine inactivates both complement and thrombin.

6. Calcium inhibits both complement and clotting. For the reactivation of prothrombin in oxalated plasma, there is an optimal concentration of calcium, below and above which clotting is retarded. Absence of calcium does not inhibit complement.

That prothrombin is not identical with complement is indicated by: 1. Alumina cream will remove prothrombin from plasma but will not alter the complement content. 2. Patients have been found whose plasma is anticomplementary, but have a normal clotting time.

Conclusion. Although a close association exists between prothrombin and complement, evidence is against the assumption that the former and the *mid-piece* of complement are identical.

7322 C

Globulin Extract of Immune Adult Serum in Prophylaxis of Measles.*

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It is widely appreciated that the majority of infants up to 3 months of age and frequently longer possess immunity to certain diseases, such as measles, diphtheria, scarlet fever, and poliomyelitis. Explanations for these facts have been varied. Most of the

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experimental data, however, points to the transplacental transmission of antigen or antibodies as being the most acceptable explanation for the presence of immunity in the new born infants. De Souza and Jorge¹ believing that the placenta may produce non-specific immune substances, utilized cord blood in the prophylaxis of measles. Their studies made during the years 1929 to 1932 showed that with 4-10 cc. of this blood they obtained 67-100% protections in 146 infants and children exposed to measles in hospital wards. Four children exposed at home and treated prophylactically developed ordinary measles. Finkelstein² had excellent results using 40-60 cc. of puerperal serum, 84.5% protections in 148 children, against 79.2% with similar doses of convalescent serum in 311 children. Others³ had less favorable results, using 20 cc. of cord blood.

McKann and Chu⁴ believed that by extracting the placenta, substances were obtained which represented maternal blood, fetal blood, and probably extracts from the placental tissue itself, whereas blood obtained from the umbilical cord represented fetal blood only, and contained only those substances involved in immunity to which the placenta is permeable. Using the globulin extract of placenta for measles prophylaxis they obtained excellent results. Forty-three susceptible children, hospitalized for other conditions, and exposed to measles, were injected intramuscularly with placental extract. In no instances did the injected placental extract fail to prevent or modify the measles in the susceptible contacts.

It was our opinion that possibly the blood contained in the placenta was the source of this active globulin extract. If that were so this immune substance should be present not only in the mother's circulation, but in the circulation of any person immune to measles, facts known to be true. We therefore extracted the globulins from the blood serum of measles immune male adults and compared the prophylactic value of this extract with the serum from which it was obtained. No attempt was made to separate off the inactive euglobulin fraction from the active pseudoglobulin.

Forty-four children susceptible to measles, 41 ranging in age from 18 months to 8 years and 3 children 12 to 14 years were exposed to measles in their homes from 2-5 days. Each child was injected subcutaneously or intramuscularly in the thigh with 8 cc. of the

¹ de Souza, J. S., *Arch. de Med. des Enfants*, 1932, **35**, 633.

² Finkelstein, G. S., *Vrach. Delo.*, 1931, **14**, 791; *J. A. M. A.*, 1932, **98**, 92.

³ Dulitskiy, S. O., *J. rann. detsk. vozr.*, 1932, **12**, 322.

⁴ McKann, C. F., and Chu, F. T., *J. Infect. Dis.*, 1933, **52**, 268. Also personal communication.

serum obtained from either of 2 donors—R. and M. Of these 18, or 41%, remained completely protected, 17, or 9%, developed modified measles, and 9, or 20%, developed unaltered measles.

Some of the above serum was then precipitated with 50% ammonium sulphate and dialized to eliminate the ammonium sulphate. The globulin obtained was then preserved with a 1/7500 solution of merthiolate and diluted with normal saline solution so that 8 cc. of the solution represented the globulin extracted from 8 cc. of the original serum. The extraction was done by Mr. Klein in the laboratory of Dr. W. H. Park. It was found to be sterile.

Twenty-four susceptible children ranging in age from 2-14 years and exposed at home for 2-5 days each injected subcutaneously or intramuscularly with 8 cc. of the globulin solution, 12, or 50%, of these remained protected, 10, or 42%, developed modified measles, and 2, or 8%, failed to be helped. The latter 2 were sisters, 4 and 14 years of age, and had been exposed 7 or 8 days. The failures were therefore to have been expected. The results with the globulin extracts of sera R and M were almost identical with those of their original sera. Since some of the globulin was probably lost in the extraction, and since the average age of the children injected with the globulin was somewhat greater than with the control serum, it is possible that the globulin fraction was slightly more effective than the serum from which it was extracted.

The injection of the globulin extract intramuscularly or subcutaneously was associated with almost immediate severe local pain, burning or gnawing in character. The pain was frequently accompanied by headache, dizziness, facial pallor, and sometimes vomiting, reactions somewhat like those following adrenalin or pituitrin injections. The pain was very severe for 15-30 minutes and continued in milder form for several hours. It was in striking contrast to the mild local discomfort following the injection of the original serum.

McKann was able to get 20 to 30 effective prophylactic doses of globulin extract from each placenta. Assuming that under conditions such as those of our study, 8 cc. of immune adult blood serum, or about 20 cc. of whole blood is an effective prophylactic dose for measles, it would indicate that the placenta contains anti-measles substance equivalent to at least that which would be obtained from 20 times 20, or 400 cc. of blood.

Although the placenta is extremely rich in blood, it is questionable whether so large a percent of it is blood, and therefore doubtful whether the presence of the anti-measles substance can be explained

on the blood-content alone. It is conceivable, however, that all of the placental fluid is comparable to blood serum and similar to it in its antibody content. It is questionable, therefore, whether it will be necessary to postulate other than humoral immunity transmitted from the mother to the placenta to explain the striking results recorded with placental globulin extract.

McKann's studies were nearly all done in hospital exposures, which according to the recent report of Schick and Karelitz,⁵ usually yields a more optimistic or exaggerated impression of the actual value of a serum. If, therefore, the dosage of placental extract will have to be larger for children intimately exposed to measles, as is the case in their homes, it is possible that their results will more nearly approximate those obtained with blood of immune adults.

Conclusions. 1. The globulin of the blood of measles immune adults carries a factor effective in measles prophylaxis. 2. This globulin extract is at least as effective as the blood serum from which it was obtained. 3. Although no direct proof is offered, suggestions are made which might explain the striking results obtained with placental globulin extract, on the basis of maternal and fetal blood contained in the placenta.

7323 C

Effect of Type of Carbohydrate on Vitamins B and G Potency of Feces Voided by Rats.*

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In a previous publication from this laboratory¹ the danger of coprophagy, as it affects the assay of vitamins B and G, was discussed. Similar observations had been reported by Roscoe.² More recently Booher and Kaneko³ have submitted data which led them to conclude that their assays for vitamin B (B₁) were not vitiated by coprophagy. The last mentioned investigators used raw corn

⁵ Karelitz, S., and Schick, B., *Wien. Med. Woch.*, 1932, **45**.

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¹ Guerrant, N. B., and Dutcher, R. Adams, *J. Biol. Chem.*, 1932, **98**, 225.

² Roscoe, M. H., *Biochem. J.*, 1931, **25**, 2056.

³ Booher, L. E., and Kaneko, T., *Proc. Soc. Exp. Biol. and Med.*, 1932, **30**, 69.