lines as is indicated by the small variance (s^2). Application of the t test[7] reveals that the differences in slopes are far in excess of the requirements for significance.

The fact that maximum growth velocity occurs with *E. coli* in the absence of any added p-amino benzoic acid if sulfanilamide is also absent does not refute the thesis of competitive inhibition. P-amino benzoic acid may be present as an impurity in the medium or more likely, it may be synthesized by the organism as required. That such amounts are very small is demonstrated by the plot of the broken lines in Fig. 1 which show how the graph would appear if 0.005 mg % of p-amino benzoic acid were present, either as impurity or as a product of bacterial synthesis, in addition to the added amount. Obviously such is not the case. However, since Rubbo and Gillespie[8] showed that as little as .00002 micrograms permitted growth of *Cl. acetobutylicum,* the amount required for growth could be present without noticeably distorting the plot. Admittedly, alternative explanations are available. Any one of a number of proposed mechanisms for sulfonamide action may obtain but it is now possible to reject all but those in which competitive inhibition is characteristic. The data presented here clearly demonstrate that sulfanilamide and p-amino benzoic acid behave as if they were competing for the same receptor site in the organism. The tremendous disproportion between the molecular concentrations merely indicates the greater affinity of the site for the p-amino benzoic acid.

Summary. Growth rates of *E. coli* were measured in the presence of sulfanilamide and p-amino benzoic acid. Mathematical analyses of the data indicate that the sulfanilamide inhibition is of the competitive type.

13243 P

Pathogenesis of Erythroblastosis Fetalis: Absence of the Rh Factor from Saliva.

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The pathogenesis of erythroblastosis fetalis has been ascribed to the isoimmunization of the mother by the Rh, or, more rarely,

[7] Fisher, R. A., *Design of Experiments,* London, 1937.

by other factors in the blood of the fetus.[1, 2] According to this concept maternal agglutinins produced in response to this stimulus after passing the placenta, act on the susceptible blood of the fetus, and thus produce the various syndromes known as erythroblastosis fetalis. This theory does not differ in principle from the older concept of "heterospecific pregnancy"[3] based on the 4 blood groups. Thus, if the property A or B in the fetus is not present in the mother, the maternal agglutinin by its action on the fetal blood was thought to induce icturus gravis, (one of the manifestations of erythroblastosis fetalis).[4] Recently it was shown by Jonsson,[5] and confirmed by Levine,[6] that in the example cited the mother's normal agglutinins may be specifically increased in titer as a result of isoimmunization.

Nevertheless, the theory of heterospecific pregnancy was abandoned because of lack of evidence.[7] Furthermore, the demonstration that the factors A and B are present, also, in tissue cells and body fluids indicate that maternal isoantibodies are specifically inactivated after passing the placenta. However, this wide distribution of the A and B blood factors applies only to about 80% of individuals (secretors) and in the remainder (non-secretors) the A and B substances are presumably limited to red blood cells.[8, 9, 10]

These facts suggested experiments to determine whether the Rh factor is also present in tissue cells or in body fluids. The tests were carried out with saliva because of its high concentration of the A and B substances.

For control, the tests, which were limited to saliva from individuals of groups A and B, were carried out simultaneously with isoantibodies anti-A and anti-B of a group O serum and an anti-Rh serum. The latter serum was obtained from a woman (Group A) who had recently delivered an infant with erythroblastosis fetalis.

Equal volumes of saliva, clarified by prolonged centrifuging and suitable dilutions of serum were incubated at 37°C for one hour and overnight in the ice-box. The tests with the anti-Rh serum — saliva

1 Levine, P., Katzin, E. M., and Burnham, L., *J. A. M. A.*, 1941, **116**, 825.

2 Levine, P., Vogel, P., Katzin, E. M., and Burnham, L., *Science*, 1941, **94**, 371.

3 Hirszfeld, L., *Konstitutionsserolgic und Blutgruppenforschung*, Julius Springer, Berlin, 1928.

4 Ottenberg, R., *J. A. M. A.*, 1923, **81**, 295.

5 Jonsson, B., *Acta Path. et Miscrobiol. Scand.*, 1936, **13**, 424.

6 Levine, P., unpublished data.

7 Koller, S., *Z. f. Rassenphysiol.*, 1930, **3**, 121.

8 Putkonen, T., *Acta Med. Fenn. "Duodecim,"* 1930, **14**, 107.

9 Schiff, F., and Sasaki, H., *Klin. Woch.*, 1932, **11**, 1426.

10 Friedenreich, V., and Hartmann, *f. Immunitätsf.*, 1938, **92**, 141.

TABLE I.
Specific Inhibition of Anti-A, Anti-B, and Anti-Rh by Saliva.

Saliva donor	Group	I Serum Group O Incubated with saliva Tested with blood suspension of group A	I Serum Group O Incubated with saliva Tested with blood suspension of group B	II Serum M.F. Anti-Rh Incubated with saliva Tested with blood O Rh+	Rh reaction
1.	A	0	++	+±	+
2.	A	0	++	+±	+
3.	A	0	++	+±	0
4.	A	0	++	++	+
5.	A*	++	++	++	+
6.	B	++	0	++	+
7.	B	++	0	++	+
8.	B	+±	0	++	+
9.	B	++	0	+±	0
10.	B*	++	++	++	+

Before adding blood, the test mixture consisted of 0.2 cc saliva and 0.2 cc serum dilution. The final dilution of the group O serum was 1:16; that of the anti-Rh serum was 1:8. Readings in I were made after the test stood 2 hours at room temperature; in II the readings were made after the test stood for 1 hour at 37°C.
*Non-secretor.

mixtures were made by adding 3 drops of a washed blood suspension of group O, Rh +. The mixtures with the group O serum were divided into 2 series, to one of which was added a group A blood-cell suspension and to the other, group B blood.

Representative experiments with the saliva of 5 selected individuals of group A and 5 of group B are recorded in Table I.

The results indicate that this technic readily reveals the presence of group specific substances A and B in the saliva. Under these experimental conditions, however, the saliva of Rh+ and Rh— individuals cannot be differentiated. These findings indicate that the Rh blood factor is not present in saliva.† Saliva samples of 63 individuals were tested (41 of Group A, 9 of whom were non-secretors, and 22 of Group B, only one of whom was a non-secretor). Of the total, 10 were found to be Rh—, 5 in each of Group A and B.

Sperm cells and seminal fluid of 3 Rh+ individuals of Group O were tested for their capacity to absorb or inhibit the action of the anti-Rh agglutinin. These results indicated that the Rh factor was not present in the material examined.

Studies on the distribution of the A and B substances in tissue cells and body fluids revealed that their presence in saliva is an index of their wide distribution throughout the body.[8, 10, 11] Ac-

† A similar observation based on several specimens of saliva was reported by Wiener and Forer (PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 215).

[11] Sasaki, H., *f. Immunitätsf.*, 1932, **77**, 101.

cordingly, there is some justification to assume that the Rh factor may be limited to red blood cells only. However, a comprehensive study of various organs and body fluids is desirable.

The absence of the Rh factor from the tissue cells and body fluids might have been anticipated on the basis of the evidence indicating the importance of the Rh factor in the pathogenesis of erythroblastosis fetalis.[12]

13244 P

Succinyl Sulfathiazole, a New Bacteriostatic Agent Locally Active in the Gastrointestinal Tract.

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Much interest has been aroused during the past year over the prospect of developing therapeutic agents that have antibacterial activity in the bowel.[1, 2, 3] A study covering 20 sulfonamides has unearthed a compound of considerable promise.

Succinyl sulfathiazole.* $COOH . CH_2 . CH_2 . CO . NH . C_6H_4 . SO_2 . NH . C_3H_2NS$, has been shown to have little toxicity when administered to dogs orally at 4-hour intervals day and night. A dosage of one gram per kilo daily given in 6 equal doses results in a fecal drug content of from 5 to 10%. Under this regimen approximately 5% of the ingested drug is excreted in the urine, and the concentration of the drug in the blood will average 1.5 mg % of sulfathiazole and 2.0 mg % of succinyl sulfathiazole. The sulfathiazole is formed by the hydrolysis of a small portion of the conjugated compound by the animal tissues and by the bacteria in the bowel. Crystals of the drug do not appear in the urine.

The antibacterial action of succinyl sulfathiazole in the bowel as measured by the effect on the coliform organisms is presented graph-

12 Levine, P., Burnham, L., Katzin, E. M., and Vogel, P., *Am. J. Obst. and Gyn.*, in press.

1 Marshall, E. K., Jr., Bratton, A. C., White, H. J., and Litchfield, J. T., Jr., *Bull. J. H. H.*, 1940, **67**, 163.

2 Firor, W. M., and Jonas, A. F., *Ann. Surg.*, 1941, **114**, 19.

3 Firor, W. M., and Poth, E. J., *Ann. Surg.*, in press.

*This compound was furnished by Sharp and Dohme of Philadelphia, Pa.