TABLE II.
Effect on Tumor Growth of 4 Intravenous Injections of Xanthopterin and of a Mixture of Xanthopterin and Leukopterin Given Over a Period of 48 Hours at 12 Hours Interval.* Seven animals were used in each group.

Group No.	Material injected	Dose, γ	Mean terminal tumor wt, mg	Standard error, mg	Significance ratio
959	Saline	—	577	42	—
956	Xanthopterin	0.5	341	21	to 959: 5.0 to 957: 5.3
957	Xanthopterin + Leukopterin	0.5 1.0	620	48	

* Female Rockland mice transplanted with Sarcoma 180; start of the experiment 10 days after transplantation; mice kept on normal diet.

containing necrotic tissue. Detailed descriptions, both macroscopic and microscopic, will be presented in a subsequent paper. Daily injections of 0.5 γ or 5γ respectively of *L. casei* factor or of 10 γ Xanthopterin were given. The animals were kept on a normal diet.

Summary. Xanthopterin inhibits tumor growth. Leukopterin does not inhibit tumor growth. It neutralizes the effect of Xanthopterin.

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Unidentified Inclusions Within the Erythrocytes in Certain Cases of Febrile Anemia.

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This brief report concerns 3 cases of progressive febrile anemia, 2 ending fatally, which were characterized by the presence within the red cells of unidentified coccoid and bacillary bodies. These were stained dark blue or bluish purple with Wright or Giemsa stains (Fig. 1). From one to 20 or more bodies were present in a single cell, and from 10 to 55% of the cells were affected. They were somewhat pleomorphic, but frequently appeared in the form of diploids, tetrads, or short batonnets, straight or slightly curved. The presence of the structures was often associated with a de-hemoglobinization of the cells; in such cases, they were clustered at the margin.

In unstained preparations, the bodies were colorless, very slightly refractile and possessed of an oscillatory motion within the cell. Treated with HCl and potassium ferrocyanide, they gave a positive iron reaction; the iron staining persisted in acid solutions, but disappeared after exposure to alkali at about pH 10. The morphology of the bodies was not altered by these procedures. They were not blackened by $(NH_4)_2S$, as is hemosiderin, nor by silver nitrate; they gave no histochemical reaction for alkaline phosphatase; the Feulgen reaction was also negative. They were resistant to autolysis, and to tryptic digestion.

By laking the blood with distilled water or saponin, it was possible to obtain a very great concentration of the bodies in the centrifuged sediment (Fig. 2). When a suspension of intact red cells containing the bodies was

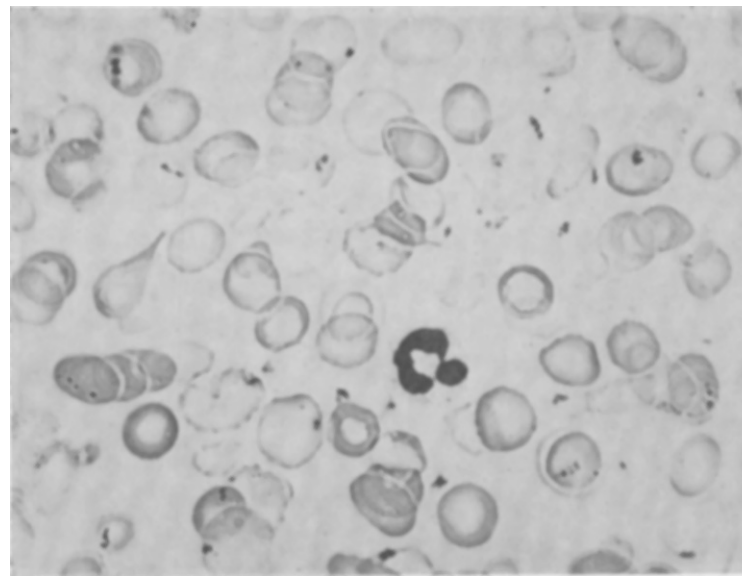

FIG. 1.
Case III. Blood Smear. Giemsa.

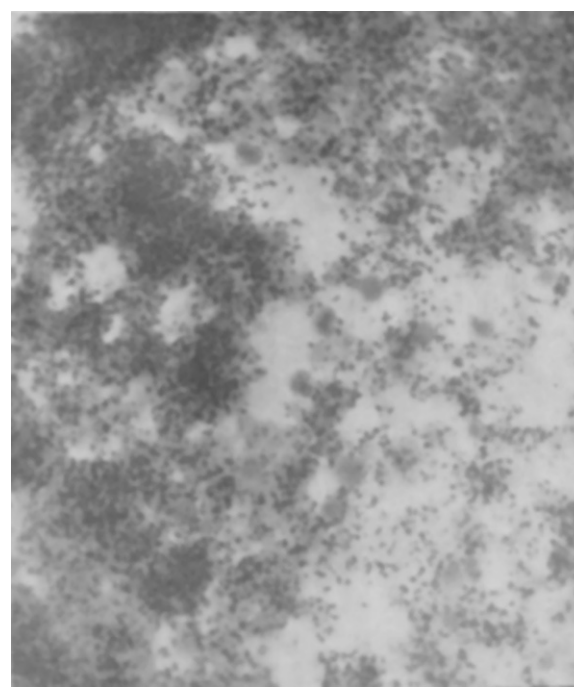

FIG. 2.
Case III. Blood laked with distilled water, centrifuged sediment stained with HCl and potassium ferrocyanide. × 460.

placed in a strong electro-magnetic field, the cells with the inclusions were drawn in a linear streak along the sharp edge of the magnet.

In Giemsa stained sections of the spleen, in all 3 cases, minute blue-staining bodies were present within the endothelial cells lining the sinuses. They were found also in reticulo-endothelial cells of lymph-nodes and bone marrow, and in Kuppfer cells, in the 2 fatal cases.

A cocco-bacillus, obtained by culture from the spleen of Case III, proved to be non-pathogenic for splenectomized monkeys, guinea pigs, rats, and mice. Its identity with the intra-corpuscular bodies could not be established, although it showed close morphologic resemblance. Cultures were not agglutinated by the patient's serum.

Blood from Case III, containing about 40% of affected cells, was injected into a splenectomized monkey, and into splenectomized guinea pigs, rabbits, mice, a bartonella-free strain of rats, and into hamsters. The animals failed to develop intra-erythrocytic inclusions, and did not become anemic or otherwise ill.

The essential clinical features in the 3 cases in which the above-described bodies appeared in the peripheral blood *only after splenectomy* were as follows:

Case I was an American-born female of 33. The duration of her illness, which ended fatally, was approximately 4 months; the symptoms were those of a progressive febrile anemia with slight icterus, and enlargement of spleen and liver. Iron, liver extract, and transfusions were ineffective, and the removal of the spleen did not influence the course of the disease. The erythrocytes reached a low count of 900,000 with 3.4 g of hemoglobin. Following splenectomy, platelets and leucocytes were elevated. Reticulocytes ranged from 20 to 26%, and there were many normoblasts. Fragility of the red cells was not altered.

Case II. A white woman, 23 years of age, the duration of whose illness was about 3 months. The clinical course and laboratory findings were similar to those of Case I; continuous spiking fever, slight icterus, enlargement of liver and spleen, and a progressive anemia which failed to respond to transfusions, liver extract, or splenectomy. The R.B.C. fell to 600,000, the Hb to 2.9 g. The reticulocytes were increased. The leucocytes were elevated until shortly before death, when a marked leucopenia rapidly developed. There was a terminal mycotic infection of pharynx, intestine, lungs and spleen.

Case III is an American boy of 19, upon whom splenectomy was performed because of an enlarged spleen and a moderately severe anemia of unknown duration which had failed to improve with the usual anti-anemic treatment. He is at present in fair condition, but his anemia has not been significantly bettered by the operation.

At the last examination, 55% of his erythrocytes contained inclusions.

In spite of intensive study, it has not yet been possible to arrive at a final conclusion as to the nature of these bodies. They are obviously not artefacts, since they can be seen in unstained fresh preparations, and can be stained by a variety of methods. In favor of their parasitic nature is their sharp staining with the Romanowsky stains, and particularly, their very frequent occurrence in diploid or tetraploid form which is strongly suggestive of active division. However, a comparison of the structures with other non-protozoan blood parasites—*Bartonella bacilliformis*,* Hæmobartonellæ, Grahamellæ, and Eperythrozoa—has led to the conclusion that they are not identical with any of these forms. *B. bacilliformis* and *Hœmobartonella muris* do not give an iron reaction when treated with HCl and potassium ferrocyanide.

If they are interpreted as parasitic organisms, one must credit them with the unique property of adsorbing or incorporating into their substance iron from the break-down of hemoglobin. The possibility that the bodies may be non-parasitic, and of the same nature as the siderous granules described by Grüneberg,[1,2] Doniach, Grüneberg, and Pearson,[3]

* Otto and Rezek (*J. Florida Med. Assn.*, 1943, **30**, 62) have recently reported the finding of similar bodies in a splenectomized male of 45, with fatal anemia.

1 Grüneberg, H., *Nature*, 1941, **148**, 114.

2 Grüneberg, H., *The Genetics of the Mouse*, Cambridge University Press, 1943, p. 163.

and by Case,[4] has been considered but no final conclusion reached.

[3] Doniach, I., Grüneberg, H., and Pearson, J. E. G., *J. Path. and Bact.*, 1943, **55**, 23.

[4] Case, R. A. M., *Nature*, 1943, **152**, 599.

Whatever their nature, the association of these intra-erythrocytic inclusions with febrile anemia resistant to all known anti-anemic treatment is of considerable interest. Further studies are in progress, and will be reported in full elsewhere.

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Hemoglobin Regeneration in Dogs Receiving a Purified Ration Plus Succinylsulfathiazole.*

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Previous studies have shown that dogs grow quite well and regenerate hemoglobin very rapidly on a sucrose-casein-synthetic vitamin ration when the casein is not highly purified;[1] that blood regeneration on mineralized milk diets is not as rapid even when extra vitamins are added,[2] and that a deficiency of certain of the B-vitamins does not always respond rapidly to administration of the missing vitamin.[3] These variations raised the question as to whether the intestinal flora might not be modified sufficiently by different rations to bring about a decreased production of some unknown factors necessary for the dog.

An attempt was made, therefore, to produce a more consistent and more severe deficiency by adding succinylsulfathiazole to the basal diet and subjecting the dog to severe phlebotomy. Growth and hemoglobin regeneration were equally as good, if not better, in the dogs receiving the drug at levels up to 4% as in the control animals. Since these results are distinctly different from those obtained in rats, we are reporting them very briefly.

Experimental. The basal diet had the following composition: acid washed casein 19%, sucrose 66%, cottonseed oil 11%, salts IV 4%,[4] and was supplemented (on a per kilo body weight per day basis) with 3 drops of haliver oil, 100 γ thiamine and riboflavin, 60 γ pyridoxine, 2 mg nicotinic acid, 500 γ pantothenic acid, and 50 mg choline.†

Eight mongrel litter mates were used, 6 of which (327-332) were put on the experiment immediately after weaning and 2 (325, 326) at the age of 2½ months. They were divided into 4 groups carefully selected on the basis of size and previous weight gains. Dogs 325, 326, 328, and 329 received the basal ration with added succinylsulfathiazole; dogs 330 and 331 were fed the basal ration with succinylsulfathiazole and 2% liver extract (1/20 powder); dog 327, a negative control, received only the basal ration, while dog 332, a positive control, received 2% liver extract (1/20 powder) added to the basal ration. The succinylsulfathiazole was mixed in the ration at a level of 0.5% for 7 weeks, then raised to 1% for 5 weeks and finally increased to 2% for another 3 weeks. Three-cc blood samples

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[1] McKibbin, J. M., Schaefer, A. E., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, 1942, **145**, 107.

[2] Potter, V. R., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, 1938, **126**, 155.

[3] McKibbin, J. M., Schaefer, A. E., Frost, D. V., and Elvehjem, C. A., *J. Biol. Chem.*, 1942, **142**, 77.

[4] Phillips, P. H., and Hart, E. B., *J. Biol. Chem.*, 1935, **109**, 657.

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