weight gains comparable with those of the controls indicating that cobalt could not be employed under these conditions in the biosynthesis of vitamin B_{12}.

It is of interest to note that the food consumption over the 15-day test period for the rats receiving 0.5 γ of vitamin B_{12} daily and those fed the unsupplemented diet but without thyroid powder were the same. The red and white blood cell counts in both the control group and in the groups receiving vitamin B_{12} fell within the normal limits.

Summary. Vitamin B_{12} counteracts the growth retarding effect of thyroid powder when fed in conjunction with a diet devoid of animal protein. The vitamin is equally effective when administered by either the oral or the subcutaneous route.

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Entrance of Intravenously Injected Sucrose into the Cerebrospinal Fluid.*

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Sucrose injected intravenously into human subjects can be recovered almost quantitatively from the urine.[1] It has been used as an osmotic diuretic drug[2] although its toxic actions greatly limit its usefulness.[3] The excretion of the sugar by the kidneys appears to result from quantitative filtration through the glomeruli, and, since the compound is very little affected by tubular reabsorption, its rate of excretion has been used to determine glomerular filtration[4] although sucrose is not apparently as satisfactory as inulin for this purpose.

Besides its action as a diuretic, it has been used in the study of body fluids. It appears not to penetrate cells readily[1] and to be contained almost solely in the extra-cellular fluid. Lavietes and his coworkers[5] have suggested that it be used to determine total extracellular fluid when large accumulations of abnormal fluid are absent. On the other hand sucrose appears to penetrate poorly into the spinal canal[6] and has been injected intravenously to reduce intracranial pressure by osmotic action.[7]

Hubbard and Anderson[8] developed a specific method for determining sucrose, injected large amounts of the sugar into human subjects who showed unusual accumulations of extra-cellular fluid, and compared the concentrations of sucrose in blood plasma and extracellular fluid samples withdrawn after various time intervals had elapsed. They found that sucrose diffused readily into extracellular

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TABLE I.
Comparison of Sucrose in Serum and Spinal Fluid.

No.	Pathological condition	Time after sucrose inj., min.	Sucrose in serum, mg per 100 cc	Sucrose in spinal fluid, mg per 100 cc
1.	Brain tumor post operative	15	134	trace*
2.	Chronic subdural hematonia	25	316	"
3.	Polyneuritis	45	212	"
4.	Subarachnoid hemorrhage. Ruptured aneurysm	60	264	4.0
5.	Cerebral thrombosis and subarachnoid hemorrhage	90	170	trace*
6.	Cerebral thrombosis	90	154	2.5
7.	Head injury with cerebral laceration	90	50	3.0
8.	Subarachnoid hemorrhage. Ruptured aneurysm	120	54	10.8
9.	Brain tumor post operative	180	22.3	trace*
10.	Encephalitis	180	30	1.0

* Approximately 0.5 mg per 100 cc.

fluid, but that equilibrium was reached slowly. The extracellular fluid formed a reservoir out of which sucrose diffused very slowly, and in one instance its presence was demonstrated in fluid and plasma 97 hours after the material was injected, while in normal subjects negative results were obtained in a much shorter time. In the 7 patients studied 20 hours or more after the sugar was given the concentration of the sugar was higher in the abnormal fluid than in the plasma.

It seemed desirable to extend the study to the equilibrium between blood and spinal fluid, for (A) a previous experiment[9] had demonstrated the presence of sucrose in the spinal fluid of a child who died shortly after an injection of the sugar, and (B) a late rise in intracranial pressure, following the initial drop, had been observed in some patients to whom sucrose had been given intravenously. In spite of the low values for spinal fluid sucrose reported by others, it seemed possible that the spinal fluid might serve as a reservoir for the sugar since such an effect had been observed in edema, peritoneal, and pleural fluids.

The method used was similar to that employed by Hubbard and Anderson.[8] 25 g of sucrose, given as 50 cc of a 50% solution were injected intravenously into 10 patients suffering from various clinical conditions. Specimens of blood and fluid were withdrawn after various periods and analyzed for sucrose. In each instance duplicate specimens were fermented, one by a strain of *Escherichia coli* which fermented all common sugars, and the other by a strain which did not destroy sucrose, but did ferment all other sugars present in body fluids. After clarification by Somogyi's zinc method[10] sucrose was determined by the resorcinol method of Roe.[11] The method gave satisfactory recovery of sucrose added to plasma and to spinal fluid, and appeared to demonstrate successfully concentrations greater than about 0.5 mg per 100 cc.

The results are given in Table I. It is evident that sucrose was present in spinal fluid in very small amounts, and that only when a hemorrhage was present could the amount found be considered significant. Even then the concentrations were so low that the authors do not believe they could explain any secondary rise in intracranial pressure, even if they had persisted until all the sucrose had been excreted from the blood by the kidneys. The figures are probably influenced by a slow diffusion of sucrose through the spinal fluid after it had entered the canal, but it seems improbable that this factor is adequate to explain the great difference between these figures and the values reported by Hubbard and Anderson for other extracellular fluids. It seems certain that, in contrast with the ease with which sucrose passes out of the capillaries into accumulations of body fluid and is filtered through glomeruli, it normally passes

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from the blood into the spinal fluid in very small amounts.

Summary. After intravenous injection sucrose occurs in the spinal fluid in very low concentration. Even when hemorrhages into the central nervous system occur, the concentration does not approach that found in blood.

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Inhibition of Development of Sarcoma 180 by 4-Amino-N^{10}-Methyl Pteroylglutamic Acid.*

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In view of the extensive developments among the anti-metabolites it was a natural consequence that cancer chemotherapy studies should be initiated with analogs of folic acid. Interest in the folic acid antagonists has been stimulated by reports of the effectiveness of Aminopterin in the treatment of leukemia (Farber).[1] In an intensive screening program during the past year a large number of analogs of folic acid and various related simple compounds have been studied against mouse leukemia[2] and various mouse and rat tumors with particular emphasis on the Crocker mouse Sarcoma 180. Thus far, one folic acid antagonist,[3] 4-Amino-N^{10}-methyl pteroylglutamic acid (A-Methopterin),† has been outstanding in its ability to inhibit the growth of Sarcoma 180. The preliminary results of the study are presented.

Materials and methods. The material was tested for ability to inhibit the growth of the Sarcoma 180 and also for its ability to damage a well established tumor.

Carefully selected tumors were cut into 2 mm cubes and implanted subcutaneously into the axillary region of groups of 5 weighed and marked white mice. In the inhibition tests, intraperitoneal injections of 0.5 cc of different doses of A-Methopterin were begun 24 hours later. In the therapeutic test, injections were begun after 3 to 7 days of tumor growth. In all instances, injections were given twice daily at 6-hour intervals for 7 consecutive days. If the animals showed definite signs of a toxic effect of the drug, administration was omitted until recovery had taken place. At the higher dosage (2.5-2.0 mg/kg/day) 3 or 4 omissions were often necessary. Below this level the drug was well tolerated.

Following the period of injections the animals were weighed and the size of their tumors determined by measurement in 2 diameters with calipers. The size of the tumors was then compared with those of the untreated controls and tumor growth was graded according to the following scheme: 1) Inconclusive, in groups of animals where 3 or more died, 2) No effect, when the largest diameter was ¾ or more of the diameter of the control tumors, 3) Moderate effect, when the diameter was ¼ to ¾ of the diameter of the control tumors, 4) Marked inhibition when the diameter was ¼ or less of that of the control tumors; actually,

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† A-Methopterin is the name given to the compound by Lederle Laboratories, to whom we are indebted for supplies. The Calco Division, American Cyanamid Company also has provided a supply of this compound.