sickle cells is rare enough that any sickle cell parent is almost certain to be heterozygous. Out of our 33 families there were 5 in which one parent had sickle cells and was type MN. Following the procedure of Finney (*4*), these may be arranged as follows:

Family	Finney Type	a	b	c	d	λ	K
7	4	3	0	0	1	6	6
8	4	1	0	0	2	3	3
11	4	1	2	1	0	0	6
17	4	0	1	0	1	−1	1
30	3	2	0	0	0	1	1
Totals						9	17

The total score (summation of λ) is seen to be 9, with a variance (summation of K) of 17. Since the total score exceeds 1.64 $\sqrt{\text{summation of K}}$, there is significant evidence against the hypothesis of random assortment, and we may consider that the existence of a linkage between the genes for sickle cells and for the M-N blood types has been demonstrated. As rapidly as possible we are adding to the collection of families.

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Spleen Extract and Tumor Growth

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The relationship between the spleen and neoplastic growth has been the subject of numerous papers, only a few of which can be mentioned here (e.g. *4*). Interest in the subject has been stimulated by the fact that primary carcinoma of the spleen has almost never been found and cannot be experimentally induced; nor is there growth of tumor tissue even when fragments are implanted directly into the organ (*1*). Metastases to the spleen from primary growths at other loci are also infrequent, and diffuse neoplastic infiltration of the spleen does not occur. The use of spleen extracts in tumor therapy has also been the subject of much controversial discussion, but that there is some definite inhibitory effect of spleen extract on tumor growth has been convincingly demonstrated by Lewisohn (*2*) and his collaborators in experimental animals.

An aqueous extract of calf's spleen has been prepared by the senior author and employed clinically by him for more than 18 years. He reported in 1929 (*3*) that two cases of Hodgkin's lesions (with and without previous X-ray therapy) showed decrease in size and softening of the nodes, but that results on other malignant growths were not encouraging. However, with improvement of techniques of extraction he has prepared a much more effective product which has been employed with decided clinical benefit, and two patients have a history of 12–13 years survival. A report of these clinical findings will be published elsewhere.

This same extract injected into mice bearing transplanted sarcoma 37 or methylcholanthrene-induced primary sarcoma produced cellular changes of a striking nature. Three concentrations were employed: "low" (8.0 grams of spleen solids/100 cc.), "medium" (15.5 grams/100 cc.) and "high" (26.5 grams/100 cc.). The difference between low and medium concentrations is merely one of an additional step in filtration. Resorption of both primary and implanted tumors was obtained, varying in percentage with the size of the tumor treated, the concentration of the extract, and the injection route employed. The best results were obtained with the medium concentration injected intraperitoneally three times daily (total daily dose, 1 cc.). The high concentration was toxic, even when injected subcutaneously; the low concentration appeared to stimulate growth. With the medium concentration, growth inhibition could be detected as early as 18 hours after the first intraperitoneal injection, and it was not necessary to resort to injection by the intravenous route. As early as 48 hours, at which time mice with transplanted tumors had received intraperitoneally 1.8 cc. of the medium concentration, almost complete degeneration of tumor cells was microscopically demonstrable. Nuclei had disappeared completely, leaving structurally intact only the cell body filled with small vacuoles. Similar phenomena were produced in about 5 days in small (5-mm. diameter), chemically induced tumors whose hosts received a total of 3.0 cc. of medium concentration spleen extract intraperitoneally. These tumors were characterized by fragmentation of nuclei and aberrant staining. With the low concentration, nuclei became greatly swollen by the end of the second day after initial injection, and this was a forerunner of increased mitotic activity. Tumors so treated grew rapidly, surpassing the dimensions of the controls. With all of the concentrations, mitosis was uninhibited as long as any viable tissue persisted. The destructive agent does not appear, therefore, to be a mitotic poison.

In Hahnemann Medical College and Hospital, three patients with malignancy and metastases (one metastatic hypernephroma and two metastatic bronchogenic carcinomas) have been injected with the Watson spleen extract (medium concentration) intravenously and intramuscularly, twice daily for 12 weeks—a total daily dose of 5–6 cc. There is definite improvement in the general health of all these patients and inhibition of progress of their tumors as revealed by Roentgen studies, made at regular intervals. Detailed clinical findings will be reported at a later date.

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