

TABLE I.

Barbiturate (as sodium salt)	Time to stop heart after 50 mg.	
	Min.	Aver. Min.
Nembutal	4	7.5
	7	
	11	
	8	
Amytal	6	9—
	9	
	11	
Luminal	9	11—
	9	
	14	
Veronal	>68	>68
	>70	
	>157	

arranged, the usual dose (50 mg.) of each of the above was added to the saline. (Temp. 19°C.) and it was shown that nembutal stopped the heart preparation in 2 minutes, whereas veronal had little or no effect after several hours.

*Conclusion.* The depressant activity of nembutal, amytal, and luminal is high compared with veronal on the sino-auricular-ventricular preparation of *Squalus acanthias*, each given as the sodium salt.

6573

### Maintenance Dose of Parenteral Liver Extract in Treatment of Pernicious Anemia.

HOWARD L. ALT.

*From the Departments of Chemistry and Medicine, Northwestern University Medical School.*

Gänsslen<sup>1</sup> and Castle and his co-workers<sup>2,3</sup> have shown that the active principle of liver (fraction G of Cohn) is much more effective when given parenterally than when given orally to patients with pernicious anemia. Since this discovery, it has been of interest to know the average frequency of injections and the amount of active

<sup>1</sup> Gänsslen, M., *Klin. Wchnschr.*, 1930, **9**, 2099.

<sup>2</sup> Castle, W. B., and Taylor, F. H. L., *J. Am. Med. Assn.*, 1931, **96**, 1198.

<sup>3</sup> Strauss, M. B., Taylor, F. H. L., and Castle, W. B., *J. Am. Med. Assn.*, 1931, **97**, 313.

principle necessary to maintain a normal blood picture in a patient with pernicious anemia. Also is this quantity sufficient to maintain perfect health and a complete neurologic remission? Murphy<sup>4</sup> states that resistant cases seem to require extract derived from 100 gm. of liver at intervals of from 5 to 7 days while uncomplicated cases could probably be maintained with injections at from 10 to 20 day intervals. He observed improvement of neurologic symptoms. Connery and Goldwater<sup>5</sup> report 4 patients who received weekly injections of an extract derived from 100 gm. of liver over a period of from 4 to 5 months. The erythrocyte counts on many occasions were below 5,000,000 per cu. mm. No progress of neurologic symptoms was noted. Strauss and Castle<sup>6</sup> observed "satisfactory results" from injections at intervals of from 1 to 2 weeks over a period of 10 months. They state that there is little uniformity in the dose required by different patients. There was no progression of spinal cord symptoms and some patients showed continuous improvement.

The purpose of the observations here reported was to determine the minimum number of injections of extract derived from 100 gm. liver that would maintain an erythrocyte count at 5,000,000 per cu. mm. in patients with pernicious anemia. Results on 4 patients who received intramuscular injections of Lederle's concentrated solution of liver extract\* (3 cc. derived from 100 gm. liver) over a period of 9 months are recorded in the chart. The grams hemoglobin per 100 cc. followed in general the curve of the erythrocyte counts and the color index was approximately unity in every case. Injections were given in the deltoid muscles of the 3 males and in the buttocks of the female patient. There was slight pain at the site of injection during and for a period of 8 to 24 hours following each injection, but there were no general reactions. During the 3 months prior to parenteral therapy, all the patients had some anemia which was probably due to inadequate oral therapy. No liver was taken by mouth after intramuscular therapy was instituted.

In the case of E. D. and W. G., the erythrocyte counts tended to fall below 5,000,000 when injections were given at 21-day intervals, whereas there was again an increase when injections were given at 14-day intervals. S. P., who received injections at 2 to 3

---

<sup>4</sup> Murphy, W. P., *J. Am. Med. Assn.*, 1932, **98**, 1051.

<sup>5</sup> Connery, J. E., and Goldwater, L. J., *J. Am. Med. Assn.*, 1932, **98**, 1060.

<sup>6</sup> Strauss, M. B., and Castle, W. B., *J. Am. Med. Assn.*, 1932, **98**, 1620.

\* The liver extract was supplied through the courtesy of Dr. G. W. Clark of the Lederle Laboratories.

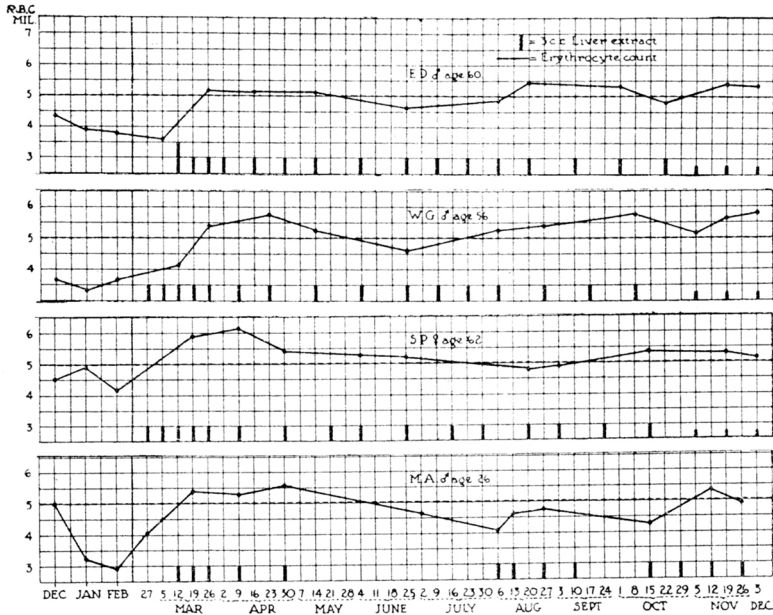


Fig. 1.

week intervals maintained an erythrocyte count at 5,000,000 per cu. mm. These 3 patients seem to have received about the minimum number of injections of extract derived from 100 gm. liver that would maintain a normal red blood cell count. The uniformity of the amount of liver given as shown in the table would undoubtedly not have been observed in a larger series of patients, especially when complicated.

TABLE I.

Period of Treatment	Liver from which extract derived	No. of injections	Ave. interval of injections
days	gm.		days
224	1400	14	16
224	1200	12	18.7
224	1200	12	18.7

Liver extract administered between March 26 and November 5, 1932.

In the case of M. A., when liver extract was stopped, the erythrocyte count gradually decreased. Later, injections at 14-day intervals were sufficient to raise the erythrocyte count to above 5,000,000 per cu. mm. The decrease noted on November 26th followed an acute respiratory infection.

At the beginning of intramuscular therapy, W. G. and S. P. showed evidence of slight cord involvement. After 9 months, W.

G. showed no progression of neurologic signs while S. P., who had marked impairment of vibratory sense in one leg before treatment, had a complete return of this function. All the patients (except M. A. when treatment was stopped) enjoyed excellent health during the period of parenteral therapy. They had no neurologic nor gastrointestinal complaints, and their weights remained constant.

In determining the minimum maintenance dose of parenteral liver therapy, it is necessary to consider the quantity of material required as well as the interval between injections. Strauss and Castle<sup>6</sup> observed maximal responses of the erythrocytes at the beginning of remission in 4 patients after a single injection of extract derived from 20 gm. liver. If a small dose at times gives a maximum effect early in the remission, a similar dose might be equally effective when used for maintenance. Two patients, E. D. and W. G. (see chart November 5th) showed increases in the erythrocyte count when 1½ cc. of extract derived from 50 gm. liver was given at 14-day intervals. Insufficient time has elapsed to know whether this dose will maintain the erythrocyte count equally as well as the larger dose.

In the routine treatment of pernicious anemia by parenteral therapy, it would seem advisable to give liver extract in excess of the minimum maintenance dose in order to allow a margin of safety in keeping the patient in a complete remission.

*Summary.* Four patients with pernicious anemia required extract derived from 100 gm. of liver at intervals of from 2 to 3 weeks to maintain a normal erythrocyte count.