Summary. The factor included in liver extract ("vitamin M") which is responsible for maintaining nutritional and hematopoietic equilibrium in monkeys is (1) apparently not identified with the following constituents as at present isolated: riboflavin, thiamin, nicotinic acid, pantothenic acid, glutamine, pimelic acid, choline, sodium paraminobenzoate, inositol and pyridoxin; or (2) if it is any of these factors, the combined administration of the above respective fractions did not result in the effect obtained with liver extract when given by the parenteral route (hypothetical "M" factor).

The administration of a yeast residue, containing, among other unknown elements, folic acid, more closely simulated the effect of parenteral liver extract than any other material we have thus far had the opportunity to test.

Liberal amounts of the basic diet and fresh water were kept in the cages at all times. The supplements were suspended in water and fed by stomach tube except liver extract which was administered subcutaneously. Diet and supplements were supplied by the S. M. A. Corporation.

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INOSITOL A TUMOR GROWTH INHIBITOR

THE importance of inositol for normal growth was established by the investigations of Eastcott,[1] Woolley[2] and others. There are no reports to date on the influence of inositol on malignant growth.

In this communication we describe the results of experiments dealing with the action of inositol on tumor growth. For these studies a rapid test for tumor growth inhibitors was employed.[3] In this test the inhibition of tumor growth is judged by comparing tumor sizes and tumor weights of treated groups of mice with untreated ones in an experimental period of 48 hours.

In Table 1 a series of experiments is presented, in which varying doses of inositol were studied. From this table it is evident that intravenous injections of inositol inhibit tumor growth, the degree of inhibition depending on the dose injected. Since September, 1942, inositol in varying doses was used in 16 experiments on 400 animals with the corresponding number of controls. The results of these experiments were similar to those presented in Table 1.

TABLE 1

EFFECT ON TUMOR GROWTH OF FOUR INTRAVENOUS INJECTIONS OF INOSITOL IN VARYING DOSES GIVEN OVER A PERIOD OF 48 HOURS*

Group No.	No. of animals in each group	Dose of Inositol γ	Mean terminal tumor weight mg	Standard error
453	11	0 (control: saline)	470	25.6
452	18	38	436	22.8
451	14	50	350	33.6
450	10	75	270	34.1
449	7	100	246	41.1
448	5	150	215	26.4
447	5	250	222	9.8
446	5	1000	142	12.8

*Female Rockland mice transplanted with Sarcoma 180; start of the experiment 8 days after transplantation; mice kept on polished rice diet for the experimental period of 48 hours.

Subcutaneous or oral administration of inositol was ineffective. Equally ineffective were intravenous injections of l-inositol,[4] inosose,[4] crystalline factors of the vitamin B-complex (thiamine, riboflavin, pyridoxine, nicotinamide, pantothenic acid, p-aminobenzoic acid, biotin and choline). Sodium phytate[4] and lipositol[4,5] showed an inhibition similar to that of inositol.

CONCLUSIONS

Inositol was found to inhibit tumor growth. The degree of inhibition depends on the dose injected. Inositol, a pure crystalline substance, can be used as a standard of reference for testing tumor growth inhibitory factors.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

NEW OBJECTIVE METHOD FOR THE DETERMINATION OF THE CIRCULATION TIME

THE determination of the circulation time in animals and human beings has generally been associated with certain disadvantages. The various tests which require subjective cooperation on the part of the patient are open to many criticisms. Some of the disadvantages are evident in the case of children, deaf mutes, moronic or mentally sluggish individuals and

[1] E. V. Eastcott, *Jour. Phys. Chem.*, 32: 1096, 1928.
[2] D. W. Woolley, SCIENCE, 92: 384, 1940; *Jour. Biol. Chem.*, 139: 29, 1941.
[3] D. Laszlo and C. Leuchtenberger, Cancer Research, 1943. To be published.
[4] We are indebted to Dr. D. W. Woolley, of the Rockefeller Institute, New York, for generously supplying us with these substances.
[5] D. W. Woolley, *Jour. Biol. Chem.*, 147: 581, 1943.

those in stupor and coma. The intravenous injection of ether, saccharin or sodium dehydrocholate carry with them not only disadvantages but even dangers.

Occasionally, some subjects whose taste buds are not fully developed may not respond in the desired measure. For that reason, objective tests have been greatly sought. These have ranged from the use of sodium cyanide, histamine, 50 per cent. carbon dioxide, alpha-lobeline ether and, more recently, the use of fluorescein. These drugs are reported to produce objective results, but, as is the case with sodium cyanide, are often open to danger. Calcium gluconate can not be used in cardiac cases that have received digitalis therapy without serious complications.

The danger of complications following the intravenous injection of many of these substances is obviated by a new objective method we have devised. This method is based on the principle that light transmitted through various translucent tissues of the body, such as the ear, finger or toe tips, or flexible skin anywhere on the body (such as that over the calves of the legs, the arm pit or the skin web between the thumb and index finger), can be detected by means of a sensitive photoelectric cell.

The injection of certain non-toxic dyes, intravenously, such as 2 to 4 cc of a 1 per cent. solution of methylene blue, or 1.0 cc of phenol-sulphon-phthalein, acts as a temporary curtain to impede the transmission of light. Interference with the transmission of light by the dye can be observed by the deflection of the indicator of a sensitive galvanometer, connected with the photoelectric cell. The time elapsing between the injection of such a dye into the vein of the arm or leg and its arrival to the point where the light and photoelectric cell have been placed, can be determined by a stop-watch, or can even be recorded objectively, by connecting the leads from the photoelectric cell to a recording galvanometer.

Thus, an objective record determination of the circulation time is made possible, which no other method affords. The fluorescein method, the safest objective method to date, is open to the criticism that several individuals may not note it at the same time. The thickness of the skin or mucous membrane and its blood content may also modify the time of fluorescent visualization. The use of a dye with a light and photoelectric cell set-up, is not only of value in determining the circulation time, but also can be used for the determination of the time required for the blood to be cleared, as demonstrated by the return of the galvanometer needle to its pre-injection point. The determination of the circulation time is recognized today to be of value in differentiating thyrotoxicosis and cardiac decompensation from other conditions which may be confused with them.

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CONTRACTION OF DENERVATED MUSCLE PRODUCED BY d-TUBOCURARINE

FROM a consideration of the physico-chemical properties and especially the polarographic behavior of the alkaloid obtained from *Chondodendron Tomentosum* (d-Tubocurarine), and other quaternary ammonium bases having high reduction potentials, it seemed very probable that the rapid intra-arterial injection of this alkaloid would cause contraction of denervated muscles. This was shown to be true for dog-gastrocnemius denervated ten days previously. A strong contraction followed the close intra-arterial injection of d-Tubocurarine. The contraction was followed by partial relaxation and terminated by a long contracture which persisted for approximately thirty minutes. During the contracture and for a considerable time after the muscle was found to be unresponsive to previously effective quantities of intra-arterially injected acetylcholine. Direct stimulation of the muscle provoked contraction during the period of curarine-induced contracture. Full details of the experiments and a discussion of their significance will be published later.

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