mouse tissue or to produce SGV disease in mice.

The character and progression of the cytopathologic changes induced in cultures of human fibroblasts by the 2 viruses which we have isolated resemble somewhat those described by Weller(12) for the varicella virus. However, the behavior of these 2 viruses in cultures differs from that of the varicella virus in that they are present in the culture fluid and can be readily transferred by the fluid. In addition the conspicuous dense granules which occur in the centers of degenerating focal lesions are not described for the lesions produced by the varicella virus.

The restricted host pathogenicity of the 2 agents also differentiates them from the virus of herpes simplex, a common virus producing a large intranuclear inclusion which might be encountered in human tissue in the absence of recognizable infection.

Conclusions. A cytopathogenic virus inducing large intranuclear inclusions like those occurring in salivary gland virus disease has been isolated from the tissues of each of 2 infants. In both cases the virus has been propagated serially in cultures of human fibroblasts derived from uterine tissue. The distinctive cytopathogenic effects and the apparent species specificity of the 2 viruses, together with the isolation of each of the viruses from human tissue which contained the characteristic inclusions of salivary gland virus disease are substantial evidence that these viruses are strains of the human salivary gland virus.

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Received May 28, 1956. P.S.E.B.M., 1956, v92.

Sedimentation Behavior of Serum Lactic Dehydrogenase. (22499)

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(Introduced by Eugene Roberts).

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The elevation of serum lactic dehydrogenase (LDH) activity has been observed in many patients with neoplastic diseases(1,2). Since 2 components with LDH activity have been found in heart(3,4) it was of interest to ascertain whether the LDH activity found in the sera of apparently healthy individuals or in patients with neoplastic diseases is attributable to one or more moieties. A technic has been described(5) which permits the determination of the sedimentation pattern of an enzyme in crude preparations. This method was applied in the present investigation to the study of the sedimentation behavior of LDH activity in serum as a first step in determining the physical properties of the serum enzyme.

Materials and methods. For investigation of sedimentation behavior one part of serum was diluted with 4 parts of saline-phosphate buffer mixture to give final solution that was 0.145M with respect to sodium chloride and

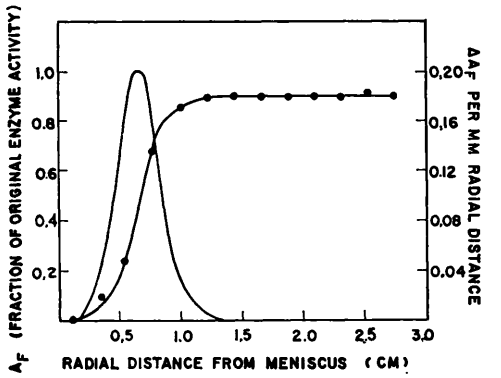

FIG. 1. Sedimentation diagram and increment curve obtained in a sampling experiment with serum lactic dehydrogenase from an apparently healthy individual (for details, see text). Sedimentation diagram, showing points determined experimentally, was plotted against left-hand ordinate and increment curve (no points) against right-hand ordinate.

0.025M with respect to phosphate (pH 7.4). For determination of sedimentation constant of LDH from erythrocytes heparinized plasma from a patient with myelogenous leukemia was centrifuged and the cells were washed with a volume of saline equivalent to original volume of plasma. Water, equivalent to original volume of plasma, was added to the washed cells. the mixture frozen and thawed 3 times. and centrifuged. The supernatant fluid was diluted 1:15 with saline-phosphate buffer mixture for investigation of sedimentation behavior. By means of a gradient pump (6), Lusteroid centrifuge tubes (1.2 x 5 cm) were filled with 4.50 ml of diluted serum or supernatant fluid from lysed erythrocytes in such a way that the fluid column within each tube contained a linear sucrose gradient ranging from 2% sucrose at bottom of tube to zero at the meniscus(5,7). Centrifugation was carried out in the SW-39 rotor of the Spinco Model E ultracentrifuge as previously described(7). At the rotational speed employed, 39,460 r.p.m., the distance of meniscus from axis of rotation was 6.09 cm. Following centrifugation, the tube contents were sampled(7), and 16 or 17 fractions consisting of successive levels of the fluid column from top to bottom were obtained. Immediately after sampling, all fractions together with original uncentrifuged solution were assayed for LDH activity by spectrophotometric method essentially as previously described(1). Reaction mixtures were incubated for 10 minutes for serum of high activity and 20 minutes for serum of low activity. Under these conditions rate of oxidation of dihydrodiphosphopyridine nucleotide (DPNH) was linear. Construction of sedimentation curves from sampling data required that the position of each point in the region of the boundaries be determined with considerable accuracy. Duplicate determinations of LDH activity, performed on each sample, gave identical results with only a few exceptions and these, on active specimens, never varied more than 1.7%. However, in the case of a few determinations on samples of very low activity the inherent error in the method gave an error as high as 5.5% in the results. Sedimentation diagrams (Fig. 1-3) were constructed from the sampling data of each experiment and translated into increment curves (Fig. 1-3) by methods previously described(5). Sedimentation constants ($s_{20,w}$) were calculated by means of standard equations(7,8). The density and viscosity of each solution were determined directly.

Results. Typical LDH sedimentation diagrams and increment curves obtained with serum are shown in Fig. 1 and 2. Fig. 3 illustrates the results obtained for LDH from a crude solution of lysed erythrocytes. The results of sampling experiments with LDH are

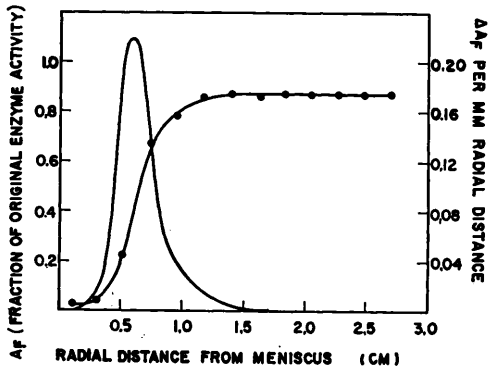

FIG. 2. Sedimentation diagram and increment curve obtained in a sampling experiment with serum lactic dehydrogenase from a patient with myelogenous leukemia (for details, see text). Sedimentation diagram and increment curve were plotted as in Fig. 1.

TABLE I. Determination of Sedimentation Constant of Lactic Dehydrogenase in Human Serum and Erythrocytes.

Centrifugation was carried out in the Spinco SW-39 rotor at 39,460 r.p.m. for 9360 sec. Solvent was .145M sodium chloride - .025M potassium phosphate, pH 7.4, containing sucrose concentration gradient ranging from zero at top of fluid column to 2% sucrose at bottom.

Source of serum	Approximate enzyme activity*	Avg temp., °C	$\Delta\chi$, cm†	$s_{20,w} \times 10^{13}$
Apparently healthy individual (non-fasting blood)	.16	23.1	.63	6.98
Idem (fasting blood), Fig. 1	.16	23.5	.67	7.20
Patient with myelogenous leukemia, Fig. 2	.77	23.2	.605	6.72
Idem (different patient)	1.28	24.8	.600	6.70
Lysed erythrocytes Fig. 3	38.0	25.0	.75	7.32

* Activity expressed as mg of DPNH oxidized/min./ml of original serum or ml of original packed erythrocytes assuming that decrease in optical density at 340 mμ of .200 is equivalent to oxidation of .1 mg of DPNH when determination is carried out as previously described(1).

† Radial distance from meniscus to peak of increment curve (see reference 5).

presented in Table I, together with the time, speed, and temperature under which the experiments were carried out. All sedimentation diagrams illustrated in Fig. 1, 2 and 3 exhibit a sharp boundary followed by a broad plateau region. The corresponding increment curves (Fig. 1, 2 and 3) consist of single, well defined peaks which are rendered somewhat asymmetric by an elevation of the leading limb.

Discussion. A major portion of the LDH activity of cancer serum was associated with a single component having a sedimentation constant ($s_{20,w}$) of 6.71 x 10^{-13} (average of 2 experiments). Normal serum and hemolyzed erythrocytes gave similar results with $s_{20,w}$ values of 7.09 x 10^{-13} (average of 2 experiments) and 7.32 x 10^{-13} (one experiment) respectively. Although there appears to be some difference between the above values, the variations are within the range of errors inherent in the centrifugation and assay methods. These values for $s_{20,w}$ are in good agreement with the following values in the literature: 7.0 x 10^{-13} reported for "heart" by Neilands(3), 6.36 x 10^{-13} and 6.48 x 10^{-13} for beef heart by Meister(4), and 7.39 x 10^{-13} for rat liver by Gibson(9). Neilands(3) and Meister(4) reported the existence of two lactic dehydrogenases from heart which differed in their electrophoretic mobility yet had the same sedimentation constant. It will, therefore, be necessary to employ other methods to determine conclusively whether the LDH activity of serum is attributable to one or more components.

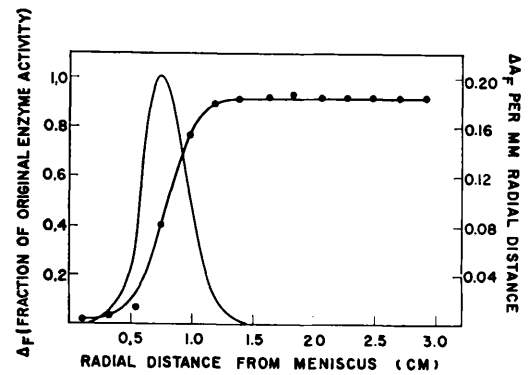

FIG. 3. Sedimentation diagram and increment curve obtained in a sampling experiment with hemolyzed erythrocytes from a patient with myelogenous leukemia (for details, see text). Sedimentation diagram and increment curve were plotted as in Fig. 1.

Summary. Lactic dehydrogenase from serum of an apparently healthy individual, sera from two patients with myelogenous leukemia, and lysed erythrocytes behaved as an essentially monodisperse compound, sedimenting at a rate which is in good agreement with that reported for the crystalline enzyme obtained from other sources. It will be necessary to employ other methods to determine conclusively whether serum LDH activity is attributable to one or more components.

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Received April 23, 1956. P.S.E.B.M., 1956, v92.

Vasopressor Effect of Synthetic 5-Hydroxytryptamine Creatinine Sulfate in Man.* (22500)

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Studies on hemostatic activity of 5-hydroxytryptamine creatinine sulfate (5-HT) indicated that administration of *small doses* of the drug into an antecubital vein caused often reflux of blood into the distal end of the plastic transfusion set, suggesting local elevation of venous pressure, while failing to affect systemic venous pressure(1). Further investigation was then undertaken on the fate of injected 5-HT(2) and on its effects on various circulatory districts.

Materials and methods. Fifty-two individuals, healthy or suffering from various diseases without elevation of venous pressure; one patient with ventricular septal defect and right to left shunt were studied. Seventy-nine experiments were performed. *Antecubital vein pressures* in one and or both arms were measured with saline manometers. On the injection side the pressure was obtained through the injection needle via a three-way stopcock during short, regular interruptions of the infusion. The system allowed separate infusions of drug or saline through the same needle. Brachial artery pressure was determined indirectly by means of aneroid sphygmomanometer. 5-*HT*§ in crystalline form was dissolved in physiological saline to prepare solutions of various strength.

Results. (a) *Local venopressor effect of 5-HT and its relation to concentration of drug.* (Fig. 1). Saline solution was first injected intravenously at a speed of 3 ml/min. for 5 minutes, without effect on the local or contralateral arm vein pressure. By different orientation of the stopcock, 3 ml/min. of 5-HT solutions of various strength were then administered for 5 minutes in 3 different sets of experiments. Injection of saline was now resumed for 15 minutes. Dose of 0.15 γ/5′ 5-HT caused negligible venopressor effect; 1.5 γ/5′ induced significant elevation of local venous pressure, lasting at least 5 minutes after the end of the infusion; a 10-fold dose (15 γ/5′) determined more pronounced and sustained response. There was no *systemic* venopressor response when a total amount of 45 γ were injected in 15 subjects (15 γ/5).

(b) *Effect of repeated or continued intravenous administration of 5-HT on local venous pressure.* Repeated intravenous infusions of 5-HT (1.5 γ/5 minutes) were given; saline solution was administered for 15 minutes between injections (Fig. 2) Venopressor response to 5-HT was progressively more pronounced as injections were repeated. Local, severe pain prevented continuation of the procedure for more than 3 times in succession. It is then not known whether decrease in local venopressor effect might, as observed in dogs

* Supported by grants from Am. Heart Assn. and National Institutes of Health, U.S.P.H.S.

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§ Kindly supplied by Dr. John Webb, Upjohn Co, Kalamazoo, Mich.