or of hemoglobin produce eosinophile migration.

Since weaker proteolytic enzymes of the order of pepsin, caroid and papain fail to eliminate the eosinophilic response, it may be suspected that protein linkage with another type of compound is involved. The procedures reported with fat solvents suggest the linkage is not with a lipid, a point further substantiated by the failure of pancreatic lipase to affect the E.S.S.

There remains the probability that the E.S.S. is a protein-carbohydrate complex. Favoring such a hypothesis is the demonstration that pepsin, ptyalin and hyaluronidase when injected alone produce an eosinophilic reaction. Both ptyalin and pepsin are prepared from biological materials and both are associated with blood group substances that are known to be mucopolysaccharides. Alternately these enzymes and hyaluronidase may release some kind of E.S.S. from the peritoneal surfaces.

It is evident from these procedures that further efforts to fractionate RBC stroma will be unsuccessful since all chemical separations will depend upon obtaining a solution of undamaged E.S.S.

Further work is under way to approach the problem through successive injections of increasingly complex proteins and of increasingly complex carbohydrates as well as to determine if the physical state of material, gel or insoluble suspensions, may determine an eosinophilic response.

The occurrence of an occasionally high eosinophile count in one of 10-20 animals may be the result of an unknown biological difference. In the course of many injections it is almost certain that trauma and peritoneal bleeding will occur from time to time. It is also possible that in spite of efforts to secure a complete mixture of solvents with the gelatinous and gummy stroma, there may not be complete contact between some portions of the mass and the solvent.

Summary. 1. A series of experiments with variously treated RBC stroma injected intraperitoneally into mice clearly demonstrates that an eosinophile-stimulating substance previously noted is not a lipid. 2. The experiments further establish that the substance is either a protein or a protein-carbohydrate compound. 3. The possibility is raised that the physical state of material (gel or insoluble suspension) may determine the eosinophilic response.

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Serum Enzyme Alterations in Cancer. (26999)

H. ALBAUM, W. ANTOPOL, B. KABAKOW, S. SLAPIKOFF, G. BLINICK, L. SUSSMAN AND L. GINZBURG

Levy Laboratories, Beth Israel Hospital, New York City, and Biology Research Laboratory, Brooklyn College, New York

Alterations of serum enzyme levels have been observed in numerous maladies(1,2,3). The fact that similar alterations in level of a particular enzyme such as lactic dehydrogenase occur in many diverse pathological lesions limits the use of a single enzyme as a specific diagnostic tool for cancer detection. The present study was undertaken to determine whether patients with various malignant tumors would reveal different patterns of multiple serum enzyme changes indicative of individual tumor types.

Materials and Methods. The serum enzymes assayed included: lactic dehydrogenase (LDH), glutamic pyruvic transaminase (SGPT), glutamic oxaloacetic transaminase (SGOT), malic dehydrogenase (MDH), aldolase (ALD), enolase (ENOL), pyruvic kinase (PK), myokinase

TABLE I. Serum Enzyme Activities[1] in Normal Controls and Patients with Malignant and Non-Malignant Diseases.

Enzyme	Normal Controls	Hernias	Benign Tumors	Cholecystitis	Cancer of Female Reproductive system	Cancer of Stomach	Cancer of Intestines
	N	N	N	N	N	N	N
LDH	26 189 ± 13.3	10 236 ± 14.4*	14 196 ± 17.0	11 306 ± 38.0*	9 615 ± 151.9*	12 312 ± 513*	49 336 ± 30*
SGPT	26 17 ± 1.0	10 14 ± 1.7	14 11 ± 1.9	11 27 ± 9.1	10 14 ± 1.8	12 11 ± 1.0*	49 24 ± 5.6
SGOT	26 15 ± .9	10 15 ± 1.7	14 15 ± 1.9	11 25 ± 5.1	10 19 ± 3.4	12 13 ± 1.1	49 23 ± 4.3
MDH	26 148 ± 13.9	10 169 ± 26.0	14 168 ± 21.6	11 201 ± 50.4	9 403 ± 69.5*	12 227 ± 39.0	49 281 ± 24.9*
ALD	25 4 ± .6	10 1 ± .4*	14 4 ± .7	10 4 ± 1.3	9 6 ± 1.3	11 3 ± 1.4	48 5 ± 1.2
ENOL	26 9 ± 1.0	10 7 ± .8	14 11 ± 1.7	11 12 ± 2.9	10 26 ± 6.9*	12 12 ± 1.6	49 17 ± 2.0*
PK	26 15 ± 1.2	10 9 ± .7*	14 13 ± 2.0	11 10 ± 2.4	10 18 ± 5.7	12 16 ± 4.9	49 11 ± .8*
MK	26 9 ± 1.3	10 6 ± .6*	14 9 ± .7	11 10 ± 2.2	10 12 ± 2.2	12 6 ± 1.5	47 11 ± 1.2
PGK	24 9 ± 1.2	10 8 ± 1.0	13 13 ± 2.5	11 10 ± 2.8	9 14 ± 2.6	12 13 ± 1.7	42 10 ± 1.5

Values shown are means together with standard errors.

[1] One unit of activity = change in density of 0.001/ml of serum/min at 24-26°C.

* The difference in means as compared with normal controls is statistically significant to the 0.05 level or more using Fisher's "t" test for significance.

(MK), phosphoglyceryl kinase (PGK), glyceraldehyde phosphate dehydrogenase (GAPDH), hexokinase (HK), creatine kinase (CK), and a combined α-glycerophosphate dehydrogenase-triose phosphate isomerase (GDH/TIM).

The methods employed for each assay have been described previously (4).

Sera were obtained from patients with various malignant lesions with metastases, non-malignant ailments requiring surgery, and from healthy hospital personnel and blood donors who served as normal controls. The age distribution in the non-cancer groups (controls consisting of normal hospital personnel, patients with hernia, cholelithiasis without infection and benign tumors) is similar to that of the cancer groups (stomach, intestine and female reproductive tract). We have also established that for at least one of the enzymes (LDH), there is no correlation between the serum level of this enzyme and age or sex. Enzyme assays were completed within 24-30 hours after collection of the blood; hemolyzed sera were rejected. Clinical diagnoses were confirmed by pathological examination of the tissue removed at operation. Sera were run independently of the diagnosis, and were correlated with diagnoses only after calculation of enzyme activities.

Results. In the initial 70 sera examined, HK, CK, GAPDH, and GDH/TIM showed little or no measurable activity in the sera of normal and diseased patients and these enzymes were consequently dropped from further study.

Preliminary results reported earlier indicated that statistically significant elevations of LDH, MDH, and ENOL activity occurred in groups of patients with cholecystitis, cancer of

the intestine, cancer of the stomach, and cancer of female reproductive organs(5,6). In this preliminary group elevations of MK and PGK occurred in cancer of the intestine and cancer of female reproductive organs. ALD was elevated in cancer of the female reproductive organs, SGPT in cancer of the intestine, SGOT in the latter 2 groups and in the group with cholecystitis. PK levels were found to be significantly lower in the cholecystitis group. Patients with benign tumors showed no significant enzyme alterations when compared to the normal controls.

Subsequently, studies were carried out on a larger group of patients, who had not received prior therapy of any kind. The data obtained from these screened groups of patients are summarized in Table I. Significant elevations of LDH occur in all of the groups except those with benign tumors. Elevations of MDH and ENOL occur most frequently in the groups with cancers of the intestine and the female reproductive organs. Significant lowering of activity of ALD, PK, and MK occurred in patients with hernias. Similarly, SGPT levels in patients with cancer of the stomach, and PK levels in patients with cancer of the intestine were found to be significantly lower. Table II

TABLE II. Observed Ranges of LDH Activity* in Normal Controls and Patients with Malignant and Non-Malignant Pathologies.

Group	N	Observed Range	Median	Mean
Normal Controls	26	63-300	210	189
Hernia	10	165-300	250	236
Benign Tumors	14	100-308	187	196
Cholecystitis	11	145-575	290	306
Cancer of Female Reproductive Organs	9	220-1400	400	615
Cancer of Stomach	12	150-700	267	312
" " Intestine	49	90-1050	268	336

* 1 unit of activity = △ O. D./ml of serum/min. at 24-26°C.

summarizes the observed ranges of LDH activity of the several groups studied. Variations in similar proportions were found in most of the enzymes studied. For example, in the group of patients with cholecystitis a range of 8-104 units of SGPT activity, with a mean of 27 and a median of 17, was observed.

Discussion. This study is not one of individual cancer patients, but rather an attempt to ascertain whether a *group* of patients with a particular tumor type has a pattern of enzyme change which is *characteristic* of the group. All of the patients in the various cancer groups had metastases, some involving the liver. The effect of specific metastases, particularly to the liver is being assessed currently. However, in the group as a whole such metastases did not appear to influence the enzyme pattern.

Patterns of alteration indicated in Table I are applicable to the group and do not necessarily reflect the finding in each individual within the group. Table II serves to highlight the fact that there is considerable variation within each group, including the normal controls. However, repeated determinations reveal a constant level in the individual controls. Among pathological groups, elevations of LDH were frequently associated with elevations of MDH, however, elevations of other enzymes occurred in an apparently random fashion.

The activities of ALD, ENOL, PK, MK, and PGK ranged upward from zero in all groups studied. Thus, it is impossible to differentiate between individuals from a group whose mean value for one of these enzymes was significantly lower from individuals whose enzyme levels are normally low.

The significance of variation in individual enzyme levels becomes apparent only when serial determinations are used as a parameter. The statistical evaluation of the data in this study indicates that a determination of enzyme level in a single sample of serum may be misleading. For example, a rise from 70 to 275 units of LD in an individual is significant even though both levels may be considered to fall within the normal range. While the values in a group of individuals might encompass a large range, the determination for any one member of the group might show little variation in contrast to that manifested by the group. This is demonstrated by the data in Table III, showing a group of normal subjects whose serum levels were repeatedly determined at different times, in some instances over a period of more than a year. From this, it is apparent that with almost all of the enzymes, each individual control tends to retain a value similar to that shown earlier.

In view of the above it would be profitable

TABLE III. Variation in Serum Enzyme Activity of Normal Controls.

			LDH	SGPT	SGOT	MDH	ALD	ENOL	PK	MK	PGK
A	obese	5/5/59	330	22	24	160	6	8	29	5	10
		12/20/60	300	26	30	200	4	11	6	6	10
B		10/10/60	135	8	11	150	0	2	2	4	4
		1/3/61	125	9	13	150	0	9	10	11	2
C		11/21/60	125	25	14	125	0	12	10	14	6
		1/3/61	110	27	14	125	1	6	6	11	4
D		10/3/60	225	17	16	200	2	8	7	6	4
		12/15/60	175	22	14	175	3	7	6	7	4
E		11/14/60	125	16	10	100	0	8	9	7	5
		1/3/61	115	16	11	100	2	6	6	10	4
F		3/4/60	175	9	10	110	4	7	9	7	5
		3/14/60	180	8	10	100	0	5	8	14	5
G	Negro	11/30/59	100	17	14	75	5	5	16	3	5
		12/19/60	85	20	16	110	0	2	6	4	4

to obtain serial determination at different times to establish the base levels for the individual. These individuals can then be followed at regular intervals and should changes occur. search could be instituted for a basic lesion responsible for this alteration. Studies in this direction have been initiated using a group of healthy hospital personnel and individuals examined at the Cancer Detection Clinic at this hospital.

Summary. Data have been presented on alterations in serum enzyme activity in patients with malignant and non-malignant diseases as compared to normal controls. Patterns of change have been established for the various groups. The patterns for the malignant groups differ statistically from those of the non-malignant ones. The malignant groups differ from each other.

Every individual in each group does not show all the changes described for the group. There is considerable overlap between pathological and control values. These discrepancies are discussed in terms of what is meant by "normal" range. Data are presented on the "normal" range of controls.

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Histochemical Evidence of Aldehyde Blocking Capacity of Lathyrogenic Agents. (27000)

VERNON L. YEAGER AND ARLEN R. SEVERSON* (Introduced by H. J. Fromm)

Department of Anatomy, University of North Dakota, Grand Forks

On the assumption that aldehyde blocking agents might produce lathyrism, Levy (1) grew salamander and toad tadpoles in water containing various aldehyde blocking agents. The greater number of those agents were found to produce tumors of the notochord. In this study an attempt has been made to determine the ability of these lathyrogenic agents to block

* National Science Undergraduate Research participant.