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.

TABLE I. Aldehyde blocking capacity and lowest effective dosage for lathyrogenesis of certain compounds.

Chemical	Molarity						Lowest concentration effective in producing tumors of notochord (Levy).	
	0	.00001	.0001	.001	.01	.1	mg/100 ml	Molarity
Phenylhydrazine	++++	++++	+	0	0	0	1	.00009
1-Methyl-1-phenylhydrazine	++++	++++	+++	+	0	0	.5	.00004
4-Phenyl-3-thiosemicarbazide	++++	++++	+++	++	−		3	.00018
Thiosemicarbazide	++++	++++	+++−	+++	+	0	10	.00110
1-Benzyl-1-phenylhydrazine HCl	++++	++++	++++	+++	+	0	1	.00004
Semicarbazide HCl	++++	++++	+++−	+++	++	+	1	.00013
BAPN	++++	++++	++++	+++	++	+−	1	.00014
Amino antipyrine HCl	++++	++++	++++	++++	++++	+++−	50	.00208
Urea	++++	++++	++++	++++	++++	++++	1	.00017
AAN	++++	++++	++++	++++	++++	++++	1	.00017

aldehydes in a histochemical test and to compare this ability with their capacity to produce lathyrism in tadpoles.

Materials and methods. Liver tissue, selected for its high glycogen content, was obtained from 4 rats, 2 guinea pigs and 5 rabbits. All were well-fed normal animals. Thin slices of liver were fixed in cold alcohol-formalin or quenched in liquid propane at −170°C and stored in acetone at −70°C for 10 days. After fixation, all tissues were embedded in paraffin. Six micron thick sections of the liver of each animal were dry mounted on slides, deparaffinized, hydrated and oxidized with 0.5% periodic acid in 70% alcohol for 10 minutes. The sections were then incubated for 1 hour at 37°C in distilled water containing serial dilutions (starting with 0.1 molar) of the following lathyrogenic agents: amino antipyrine HCl, phenylhydrazine HCl, semicarbazide HCl, urea, aminoacetonitrile hydrogen sulfate (AAN)†, and beta-aminopropionitrile (BAPN). Because of low solubilities, serial dilutions of a saturated solution of 4-phenyl-3-thiosemicarbazide were used while 1-benzyl-1-phenylhydrazine HCl was dissolved in 70% alcohol. Control sections of each liver were incubated in water or 70% alcohol. As in Levy's experiment, the pH was not adjusted. After incubation all slides were rinsed with distilled water, stained for 30 minutes in Schiff's reagent, rinsed in sulfurous acid, washed in running tap water for 10 minutes, dehydrated, cleared, and mounted in Permount. The staining reaction for each slide was then graded using 4+ when full staining was present and zero when total blocking of staining had occurred.

Results. The results are shown in Table I where the compounds tested have been arranged in order of their capacity to block the histochemical aldehyde-Schiff reaction. The table also shows the minimum concentration of the compounds shown by Levy to be effective in producing tumors of the notochord, and a) that the compounds differ widely in their ability to block aldehydes and b) their ability to block aldehydes *in vitro* differs from their ability to produce tumors of the notochord in tadpoles.

Discussion. Although an agreement of the results of this study and the study of Levy would have been good supporting evidence that the mechanism of lathyrogenesis is aldehyde blocking, no such agreement exists. However, the differences observed in the 2 experiments may be due to inherent differences between *in vitro* and *in vivo* studies. Because urea(2) and AAN showed no aldehyde blocking capacity, this study suggests that the lathyrogenic compounds may have some other characteristic in common which may be responsible for production of lathyrism in tadpoles.

Summary. This study has demonstrated that compounds known to possess lathyrogenic

† Generously furnished by Abbott Laboratories, North Chicago, Ill.

properties may, or may not, block the periodic acid-Schiff reaction, and that for these compounds, no correlation exists between their aldehyde blocking capacity and their ability to produce lathyrism in tadpoles. The mechanism by which those compounds produce lathyrism therefore continues to be obscure.

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"Epithelial Transformation" of Human Synovial Connective Tissue Cells: Cytologic and Biochemical Consequences. (27001)

C. WILLIAM CASTOR, ROBERT K. PRINCE AND EMILY L. DORSTEWITZ
(Introduced by Burton L. Baker)
Department of Internal Medicine and Rackham Arthritis Research Unit,† University of Michigan Medical School, Ann Arbor

While it is generally recognized that cells cultured *in vitro* may undergo "alteration" during the course of serial propagation, the precise nature of the observed changes remains obscure. One distinctive pattern of alteration is well illustrated by the 8 Detroit strains of human epithelial-like cells(1). In these cell lines, cultures of fibroblast-like cells derived from bone marrow, pleural and ascitic fluid, developed plaques of cells characterized by an epithelial growth pattern, rapid multiplication, giant nucleoli, and polyploidy. Since cell lines which accomplish this "transformation" are sometimes capable of extended propagation *in vitro*, they provide a system which can be studied on a mass scale over a prolonged interval. Under these circumstances, the cellular system might be used to study "retained" structural and biochemical characteristics on the one hand, while on the other hand this system may unfold for critical scrutiny the biochemical alterations and related changes in morphology that provide the new cell with an improved outlook for survival in the abnormal environment of the culture flask.

The present report describes the cytologic and biochemical consequences of a fortuitous "epithelial transformation" of a cell population derived from human synovial tissue. In previous investigations, microscopic examination of primary outgrowth from normal and malignant synovial tissue revealed cells with fibroblast-like morphology(2,3), while functional studies have demonstrated the capacity of these cells to form mucopolysaccharides(4, 5,6,7,8,9). In view of the biochemical changes documented in this communication, one might hope that understanding of such "transformations" would be advanced by systematic study of biochemical parameters in addition to the usual microscopic observations.

Materials and Methods. Synovial tissue was obtained by needle biopsy from the knee-joint of a 50 year-old man with rheumatoid arthritis of 6 months duration. This diagnosis was supported by clinical examination, x-ray evidence, a Latex fixation test for rheumatoid factor positive in a titer of 1/5120, and by the pathologic interpretation of the biopsy itself. At another hospital the patient had had a 10-day course of treatment with triethylenemelamine. Explantation of tissue fragments was carried out in T-flask under perforated cellophane as described earlier(9). Establishment of monolayer cultures, feeding schedules, and harvesting techniques were carried out as in previous studies(9).

Cell enumeration and volume measurements were carried out with a model B Coulter Electronic Cell Counter and Cell Size Analyzer. Hyaluronic acid was measured in culture medium as uronic acid by the method of Bollet as well as by a method developed in this laboratory(10,11). Hexose was determined by

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