labelled procursors and under identical conditions, embryonic or normal skin did not release any labelled deoxyuridine into the medium, although comparable amounts of the labelled precursors were taken up by the embryonic skin from the medium. Normal skin took up only negligible amounts of the label.

Conversion of deoxyuridine into thymidine involves several factors and these studies do not clearly indicate what causes deoxyuridine release into the medium. The observation that either aminopterin or B_{12} and folic acid do not change the magnitude of deoxyuridine released into the medium, however, suggests that the enzyme which converts deoxyuridine into thymidine is lost in these tumor cells.

In chemotherapy of tumors only those antimetabolites can be used whose normal counterparts are extensively utilized by the tumor but not by normal cells. A search for such agents can be done by a chromatographic system which has been adopted in this study and which is simple and rapid. A study of alternate pathways and evaluation of their relative importance is vital for selecting a step in a biosynthetic pathway where the chemotherapeutic agent will be most effective. For example, the folly of use of deoxyuridine or uridine antimetabolites for chemotherapeutic purpose in case of tumors which release or do not use these precursors for DNA synthesis is demonstrated by these studies.

Table III. De novo formation of labelled uridine from orotic acid-2-C^{14} in DR- and WR-papilloma and Vx-2 carcinoma

Tissue	Orotic acid-2-C^{14} uptake (nmoles/ml)	Labelled uridine released (nmoles/ml)
DR-papilloma		
1	4.67	0.359
2	4.48	0.307
WR-papilloma		
1	5.73	0.703
2	5.82	0.89
Vx-2 carcinoma		
1	5.72	0.042
2	6.34	0.019

Orotic acid-2-C^{14} used had specific activity of 7.2 μc/mg.

Zusammenfassung. Virusinduzierte Tumorzellen geben im Gegensatz zu normalen Hautzellen Deoxyuridin ins Medium ab.

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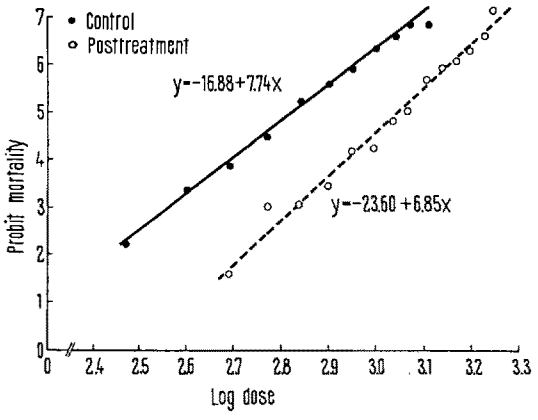
Recovery Effect of Serotonin-Creatinine Sulfate Complex on X-Irradiated Planarians

Several hypotheses have been proposed to explain the radio-protection afforded by serotonin-creatinine sulfate complex (5-HT)[1,2]. Since radiosensitivity in organisms depends as much on the alteration of critical structures as on the restoration of recovery mechanisms, in this communication it is shown that 5-HT may play an important role not only in radio-protection, but in the restoration of recovery mechanisms. The planarians (*Dugesia dorotocephala*) used in the experiments were collected from a pond on the grounds of the botanical garden of the Universidad Nacional Autónoma de México. Planarians were maintained at room temperature in dishes containing electro-purified water and were fed fresh liver twice a week. No natural deaths were recorded.

The control (C) and posttreated (P) groups were irradiated in small petri dishes containing electro-purified water. After irradiation, P-planarians were submerged for 1 h in a solution of serotonin-creatinine sulfate complex (Hycel, Houston, Texas) at a concentration of $3.14 \times 10^{-5} M$ and were then transferred to electro-purified water in regular dishes. After irradiation, C-planarians were returned to electro-purified water in regular dishes too.

Total exposures from 300 to 2000 Roentgens (R) were applied to groups of 40 planarians. Mortality data were recorded daily for 60 days. A Siemens Stabilipan apparatus was used as a source of X-irradiation. Operating at 250 KV and 15 mA and with a 0.5 mm Cu filter at a distance of 40 cm from the subject, it gave a dosage rate of 117 R/min.

The mortality data of C and P groups are illustrated in the Table. The usual sigmoidal dose-mortality curve was obtained. The dose giving 50% mortality in 60 days ($LD_{50/60}$) for group C was 676.1 R (limits 646.5–707.1) and for group P was 1140 R (limits 1104–1177), obtained by Probit analysis (Figure).



Probit analysis of X-rays irradiated planarians with and without posttreatment of serotonin-creatinine sulfate complex (5-HT).

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The Dose Reduction Factor (DRF) at the $LD_{50/60}$ level was 1.65, demonstrating that 5-HT facilitated the planarians' recovery from X-rays.

Many radioprotectors have been described in the literature, but only a few substances applied after irradiation decrease the effects induced by radiation. NERURKAR et al.[3] and SAHASRABUDHE[4] showed that methionine applied after irradiation is effective in recovery of nucleic acid synthesis, but BACQ and BEAUMARIAGE[5] considered it insufficiently important to affect mortality. KANAZIR et al.[6] and BEĆAREVIĆ et al.[7] found that X-irradiated rats treated with nucleic acids survived lethal doses of radiation. BEĆAREVIĆ and his collaborators interpreted this recovery effect as a depression of the cellular metabolic rates of the irradiated rats or as a result of the inclusion of biologically active nucleic acids which would permit the recovery of metabolic processes.

Percent of mortality in planarians at different dose of X-rays with and without posttreatment of serotonin-creatinine sulfate complex

Exposure in Roentgens (R)	Mortality (%)	
	Control	Post-treated
300	0	0
400	5	0
500	10	0
600	25	2
700	60	2
800	72	5
900	82	22
1000	92	22
1100	95	42
1200	97	52
1300	97	77
1400	100	82
1500	100	85
1600	100	90
1700	100	95
1800	100	100
2000	100	100

SUGAHARA et al.[8] found that precursors of nucleic acids increase the survival time of mice receiving repeated sublethal doses, but the recovery effect seemed to be limited to sublethal damage.

When dormice (*Glis glis*) were exposed to lethal dose of X-rays during hibernation and cysteine was injected when the animals were brought 3 weeks after irradiation to room temperature, no mortality occurred within the following 30 days[9]. Cysteine and cysteamine applied after irradiation to swell the seeds of *Vicia faba*, reduced the mitotic inhibition[9].

In our experiments 5-HT applied after irradiation in planarians demonstrated its efficacy in restoration of the recovery mechanism altered by X-rays.

Resumen. En este trabajo, se demuestra que el complejo de serotonina-sulfato de creatinina (5-HT) no solamente es un radioprotector efectivo de las planarias contra los rayos X, sino que también interviene en la restauración de los mecanismos de recuperación cuando se aplica como postratamiento a la irradiación.

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Growth Inhibitory Effects of Adenosine 3′,5′-Monophosphate on Mouse Leukemia L-5178-Y-R Cells in Culture

The importance of adenosine 3′,5′-monophosphate (cyclic AMP) in normal cell functions and metabolism is becoming increasingly apparent in many tissues and organs[1,2] and it has been recently reported to inhibit the growth of transplanted NKL-lymphosarcoma in mice and the multiplication, as measured by viable counts, of tumorigenic cell lines in vitro[3–5]. However, the mechanism by which cyclic AMP inhibits the cancer cells is at present unknown.

During our study of the inhibitory action of heat-inactivated antisera, in the absence of complement, on mouse leukemia L-5178-Y-R cells in culture, we found cause to speculate that some indirect mechanisms triggered as a result of antibody-antigen reactions on the cell membrane might be involved[6]. Growth inhibitory effects of the antisera are of a rather slow process, as are those of hormonal effects on the cells, starting at 4 to 6 h after the experiment, with maximal effects at 24 to 48 h. Systems around pyruvic acid cycle seem to be involved. Glucose, succinate, nicotinamide, but not malate, are able to alleviate, at least partially, the harmful effects of antisera. These phenomena are very reminiscent of the second messenger effect found in hormonal systems. Furthermore, activation of adenyl cyclase in the sea urchin egg membranes has been reported at fertilization[7]. We, therefore, investigated whether cyclic AMP would mimic the effects of antisera on L-5178-Y-R cells. The results are remarkably similar.

We now report the effects of cyclic AMP on the mouse leukemia L-5178-Y-R cells in culture. The experimental method used was the combination of the previously reported[6] and that of the modified BOLLUM's[8,9]. Two