The simple experiments reported here leave unanswered many questions regarding the nature of the Sendai virus CFF. However, to solve the practical problem of achieving a high proportion of heterokaryons in systems where cell fusion occurs with difficulty, we suggest using freshly harvested allantoic fluid and avoiding any concentration of virus since this seems to have the opposite effect on the CFF. Careful control of the UV dose is also mandatory. Moreover, our experience has convinced us that each different mixture of cells that one wishes to use for fusion must be approached as a new experiment for which optimal conditions (cell concentrations, proportions, virus dose) must be found.

Summary. Induction of high levels of cell fusion by UV inactivated Sendai virus depends both on the virus preparation and the types of cells being fused. Studies on the optimal UV dose reveal a biphasic effect on the viral cell fusion factor (CFF). Other studies show that the CFF is very labile, is separate from both the hemagglutinin and the virion itself, and, therefore, is partially lost by the usual methods of viral concentration. Optimal conditions for inducing cell fusion by Sendai virus are described.

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Effect of Regional Shielding on Plasma Enzyme Changes in Rats after 800 R X-Irradiation (33442)

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(Introduced by Paul D. Altland)

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In previous studies (1–3), it was found that rats show a moderate rise in plasma glutamic oxalacetic transaminase (PGOT) at 6 hr and a marked fall in plasma alkaline phosphatase (PAkP) at 2–9 days after whole-body X-irradiation. To determine the possible origin of these plasma enzyme changes, the effect of shielding with lead various regions of the body during such an exposure was studied.

Materials and Methods.[1] Young adult male Sprague-Dawley rats weighing 200–350 g were used in a series of experiments. In each experiment, 10–14 animals were divided into a control group that was not irradiated, an irradiated group that was not shielded, and one or more regionally shielded groups. All rats in a given experiment, including nonirradiated controls, were anesthetized by intraperitoneal injection of sodium pentobarbital, 50 mg/kg, during the period of irradiation.

Irradiations were carried out at 23° with an X-ray unit operated at 300 kvp and 20

[1] The "Principles of Laboratory Animal Care" as promulgated by the National Society for Medical Research were observed during this study.

ma with added filtration of 2 mm Cu. The TSD was 55 cm and the average dose rate 105 R/min. The rats were exposed to 800 R one at a time and were placed in a supine position in a lucite frame open toward the X-ray beam. The limbs of the anesthetized rat were loosely fixed in an extended position by a loop of adhesive tape with ends attached to the frame on both sides. Strips of lead, 0.5 in. thick, were laid on the rectangular side arms of the frame to shield selected regions of the body. For example, to block irradiation of the entire abdomen, the strips were placed on the side arms of the frame so as to shield the body of the rat from the tip of the xiphoid to the symphysis pubis. To shield the upper abdomen, the strips extended from the tip of the xiphoid to the lower costal margin. Necropsy revealed that this shielded upper abdominal region included virtually the entire liver and stomach, except the distal pylorus, but only a small or insignificant portion of the spleen, kidney, or intestines.

The animals were housed in a room maintained at 23° and were given Purina Laboratory Chow and water *ad libitum*. The rats were bled by cardiac puncture under ether anesthesia immediately before sacrifice, by means of heparinized syringes and tubes. In some experiments, the rats were bled at 6 hr after irradiation for PGOT determinations, and in other experiments at 4 days after irradiation for PAkP determinations. Each rat furnished one plasma sample. PGOT determinations were made at 505 mμ and alkaline phosphatase at 410 mμ, using materials and procedures obtained from the Sigma Chemical Company (4) and a Coleman Junior spectrophotometer.

Histologic studies were made on a limited number of animals by methods described in a previous paper (3).

Results. Results are summarized in Tables I and II. X-irradiation of unshielded animals caused a significant rise in PGOT at 6 hr and a marked fall in PAkP at 4 days. The changes were comparable to those described previously (3). When only the abdomen was irradiated, the fall in PAkP at 4 days was comparable to that in unshielded animals, but the rise in PGOT at 6 hr was less pronounced.

TABLE I. Plasma GOT Values in Controls and in Rats Bled 6 Hours after 800 R.

Group	No. of rats	PGOT (units/ml)
Control	29	85 ± 4 [a]
Unshielded	43	112 ± 4
Entire abdomen shielded	32	85 ± 3
Upper abdomen shielded	7	109 ± 5
Lower abdomen shielded	13	102 ± 7
Only abdomen irradiated	20	101 ± 5

[a] Mean ± SE.

Shielding the entire abdomen prevented or greatly diminished the rise in PGOT at 6 hr after X-irradiation (Table I) and the fall in PAkP at 4 days (Table II). Shielding only the upper or only the lower abdomen reduced moderately the fall in PAkP at 4 days, but had little or no effect on the rise in PGOT at 6 hr.

Histopathologic studies revealed the presence of X-irradiation changes in the lymph nodes and other radiosensitive organs in unshielded regions and confirmed the effectiveness of shielding.

Discussion. The rise in GOT at 6 hr after irradiation has been correlated in time with severe pathologic changes in the lymphoid tissue, spleen, intestinal mucosa, and bone marrow, and these tissues have been considered to be the major source of the excess GOT in the plasma (2). According to this hypothesis, the PGOT values rise less after

TABLE II. Plasma Alkaline Phosphatase (PAkP) Values in Controls and in Rats Bled 4 Days after 800 R.

Group	No. of rats	PAkP (units/ml)
Control	21	6.1 ± 0.4 [a]
Unshielded	31	0.9 ± 0.05
Entire abdomen shielded	12	4.5 ± 0.6
Upper abdomen shielded	12	2.7 ± 0.4
Lower abdomen shielded	16	3.7 ± 0.5
Only abdomen irradiated	13	0.7 ± 0.05
Upper abdomen irradiated	12	7.1 ± 0.8
Lower abdomen irradiated	14	2.2 ± 0.1

[a] Mean ± SE.

irradiation of the abdomen alone than after whole-body irradiation (Table I) because of the less extensive tissue damage in the abdominally irradiated animals. If this were the only factor involved, however, a similar intermediate rise in PGOT above values in nonirradiated rats would be anticipated in abdominally shielded animals because of excess GOT derived from damaged radiosensitive lymphoid and hematopoietic tissue in the extraabdominal unshielded regions. Since no such rise above normal values was found (Table I), this suggests that the radiosensitive lymphoid and hematopoietic tissues are not the sole source of the excess PGOT and that additional tissues and factors may play a role.

In previous studies, a rise in GOT and certain other enzymes in the serum was induced in rats by a 5-hr exposure to arduous exercise (5) or to a simulated high altitude (6) or cold environment (7). Such changes were found even in animals showing no significant histopathologic changes. The rise was attributed to a widespread increase in cellular permeability, involving even some tissues appearing histologically normal, allowing certain intracellular enzymes to enter the circulation in amounts exceeding the capacity of the body to catabolize or the plasma to inactivate them (8). It has been postulated (3) that X-irradiation may initially induce in rats a similar widespread increase in cellular permeability. The marked effect on the PGOT values of either irradiation or shielding of the abdomen suggests that this postirradiation change may be, at least in part, an indirect effect of abdominal irradiation, perhaps due to increased absorption of endotoxins (9) from the irradiated gut or to an electrolyte imbalance (10).

It is well known that fasting will cause a marked fall in alkaline phosphatase in the rat (11). However, the fall in alkaline phosphatase after irradiation in this study is relatively much greater than that reported in previous studies (7, 12) in rats fasted overnight. Moreover, other investigators (1) have found a greater fall in PAkP in X-irradiated rats than in pair-fed nonirradiated controls. These findings indicate that a fall in PAkP in X-irradiated rats is not due merely to limited food comsumption. The PAkP in man and other mammals is a mixture of alkaline phosphatases derived from various organs, chiefly the skeleton, hepatobiliary system, and the intestines (11). In the rat, the greatest portion is derived from the intestine (13). Since abdominally shielded rats showed no marked fall in PAkP after X-irradiation of the extra-abdominal skeletal system, it is unlikely that the marked fall in PAkP in X-irradiated rats is due to a greatly reduced contribution of skeletal alkaline phosphatase to the circulation. Since irradiating the liver in the upper abdomen did not cause a fall in PAkP (Table II), it is evident that the fall in PAkP after X-irradiation is not due to a marked suppression of the hepatobiliary contribution of PAkP. These findings suggest that the fall in PAkP in irradiated rats is due largely to a reduced contribution of alkaline phosphatase to the plasma by the intestines. This conclusion is supported by histochemical studies demonstrating a reduction of alkaline phosphatase in the gut mucosa during the postirradiation period corresponding with the low PAkP values (14).

Summary. Groups of unshielded and regionally shielded rats were exposed to 800 R X-irradiation and compared with nonirradiated controls. As reported in an earlier study (3), unshielded rats showed a moderate rise in plasma glutamic oxalacetic transaminase (PGOT) at 6 hr and a marked fall in plasma alkaline phosphatase (PAkP) at 4 days after irradiation. Shielding the abdomen prevented or greatly lessened these changes. Irradiating only the abdomen produced a relatively moderate rise in PGOT at 6 hr but caused a marked fall in PAkP at 4 days after irradiation comparable to that found after whole-body X-irradiation. It is suggested that the rise in PGOT is derived in part from excess GOT released from overtly damaged lymphoid and other radiosensitive tissues and in part from other tissues due to a widespread initial increase in cellular permeability induced by X-irradiation. The fall in PAkP is attributed to a reduced contribution of intestinal AkP to the circulation due to radiation injury to the intestinal mucosa.

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Inhibition of Adjuvant-Induced Polyarthritis with Cytarabine (33443)

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Adjuvant-induced polyarthritis is thought to be a "delayed hypersensitivity" disease (1, 2). It is characterized by proliferative joint disease and a variety of other clinical features. It has many features characteristic of Reiter's disease in man (3). Various workers (4–7) have shown inhibition of the disease with so-called immunosuppressants and cytotoxic drugs. Nonsteroidal and steroidal anti-inflammatory drugs inhibit adjuvant-induced polyarthritis differently. The nonsteroidal anti-inflammatory drugs ameliorate the systemic inflammatory component; without altering the course of the disease. The steroidal drugs inhibit the onset, severity, and progression of the disease by depressing the reactivity of the draining lymph nodes primarily and the inflammatory phases of the systemic disease secondarily (7).

Cytarabine depresses bone marrow function, inhibits antibody formation and is cytotoxic to various cells when added *in vitro* (8–11). Its effects on adjuvant-induced polyarthritis of rats were studied and these form the basis of the present report.

Methods. Adjuvant arthritis was produced by the inoculation of 0.5 mg of *M. butyricum*[1] in 0.1 ml of mineral oil directly into the tail of Sprague-Dawley male rats of the Badger colony (12–18). Animals usually develop arthritis within 14–20 days and are either scored visually and/or the acute phase reactants in the serum (19) are studied simultaneously; in order to ascertain the inhibitory effects of drugs.

The various other procedures (granuloma pouches, antipyretic and antihindpaw edema assays) have been summarized (20). Cytarabine and the other drugs were given as indicated in the Tables I–VIII.

Results. Cyclophosphamide and cytarabine do not possess local anti-inflammatory effects when injected directly into the granuloma pouches of rats. Hydrocortisone, used as additional controls in these studies, inhibits exudate formation in granuloma pouches (Table I). 5-Fluorouracil and 2-amino-6-mercaptopurine, but not 6-mercaptopurine, inhibit inflammatory exudate formation into granuloma pouches.

When given orally, cyclophosphamide and phenylbutazone depress the elevated temperatures of rats with yeast-induced fevers, but cytarabine shows no activity (Table II).

[1] Phenylbutazone was obtained from Geigy; Medrol from Upjohn; Cyclophosphamide from Mead Johnson; and *M. butyricum* from Difco.