

THE CYTOGENETIC EFFECT OF SLOW NEUTRONS*

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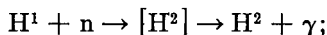
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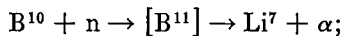
THE study of the biological effect of different radiations has progressed as sources of the various radiations have been developed. The effects of X, gamma, beta and alpha rays, of protons and fast neutrons, and recently of fission fragments have been studied in numerous organisms, both plant and animal. Before the development of the nuclear reactor, however, there was no source of slow neutrons in the amounts necessary for a study of biological effect.

The fast neutrons from uranium fission can be moderated by elastic collision with graphite or heavy water in a nuclear reactor until their velocity is reduced to that of thermal energies (average 2200 meters/sec = 0.025 electron volts); such very slow neutrons are called thermal neutrons. Unlike fast neutrons, whose principal reaction with matter is one of scattering, thermal neutrons because of their very low energy and velocity are more likely to be captured than scattered by the atoms they encounter. Most of the reactions of biological elements with thermal neutrons are capture reactions. After an atom captures a neutron, it forms a new compound nucleus with an excess of energy. This new compound nucleus may then:

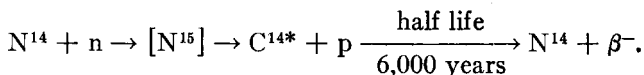
- 1) emit a gamma ray immediately to form a stable isotope, e.g.,¹



- 2) emit a heavy particle immediately to form a stable isotope, e.g.,



- 3) emit immediately a capture radiation to form a radioactive daughter which subsequently emits beta or gamma rays at a rate characteristic for the isotope formed, e.g.,



It is the immediate or "capture" radiations and the delayed or "decay" radiations which are ionizing and produce the effect; thermal neutrons, of themselves, apparently produce no effect since their kinetic energy is too low to produce recoil nuclei by elastic collisions in matter and since they are uncharged particles.

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¹ These nuclear reactions are usually given in an abbreviated form much like chemical reactions. The reaction $\text{H}^1 + \text{n} \rightarrow \text{H}^2 + \gamma$ is abbreviated to $\text{H}^1(\text{n}, \gamma)\text{H}^2$.

It appears that the biological effect from thermal neutron exposures would be due to two components of the ionization dose—electromagnetic radiation (gamma rays) and particulate radiation (protons and alpha particles). One of the striking biological effects of radiation is the production of chromosomal aberrations, which has been studied extensively in the plant *Tradescantia*. It has been known for some time from *Tradescantia* studies that the yield of chromosomal aberrations is different when electromagnetic and particulate radiations are used (for the same ionization dose, particulate produces more aberrations than electromagnetic radiation). In addition, the yield of “two-hit” or exchange aberrations differs qualitatively for the two types of radiations. With electromagnetic radiation of high intensity, the yield of these exchange aberrations increases as the square of the dose, indicating that each of the two breaks involved in the production of an exchange aberration is produced by a different electron track. With particulate radiation, however, the yield of exchange aberrations increases linearly with dose, indicating that both breaks are produced by a single particle (review in LEA 1947). This background of information on the differences in response to electromagnetic and particulate radiation made *Tradescantia* an appropriate choice for a study of the qualitative and quantitative biological effect of thermal neutron radiation from the Oak Ridge pile.

PHYSICAL METHODS

Material was exposed to thermal neutrons in a treatment facility especially designed for biological experiments with the object of obtaining the highest intensity of thermal neutrons and the smallest amount of fast neutron and gamma-ray contamination possible. A drawing of this facility is shown in figure 1. The arrangement was in part dictated by other uses of the thermal column. The bottom of the drawing is the position of the uranium-graphite lattice of the pile itself. Above this is an eight-inch layer of bismuth bricks interposed to eliminate the fission gamma rays. Above the bismuth bricks is the thermal column, a seven-foot-tall by six-foot-square column of graphite. In the center of the thermal column and on the center line of the pile is a bismuth “safe”; the central cavity of the bismuth safe is the treatment position. Specimens are inserted and removed from the treatment space by means of a sliding graphite rod with a bismuth plug on the end, to which is fixed a graphite treatment box containing the specimens. When the box is in the treatment position, it is completely surrounded by bismuth. A drawing of the graphite treatment box is shown in figure 2. Specimens were always placed on the “slope” of the box, the lowermost face when the box was in the treatment position. Ventilation of the treatment space is assured by grooves and slots through which air passes in from the outside, down the exit-entry tube into the bismuth safe, and out into the pile through ventilation holes in the safe; the pile is at negative pressure. Temperature inside the safe is room temperature.

Measurements: The method by which a neutron flux (the number of neutrons crossing a square centimeter per second) is measured is based on the fact that when neutrons are captured a radioactive isotope is formed. Other things being

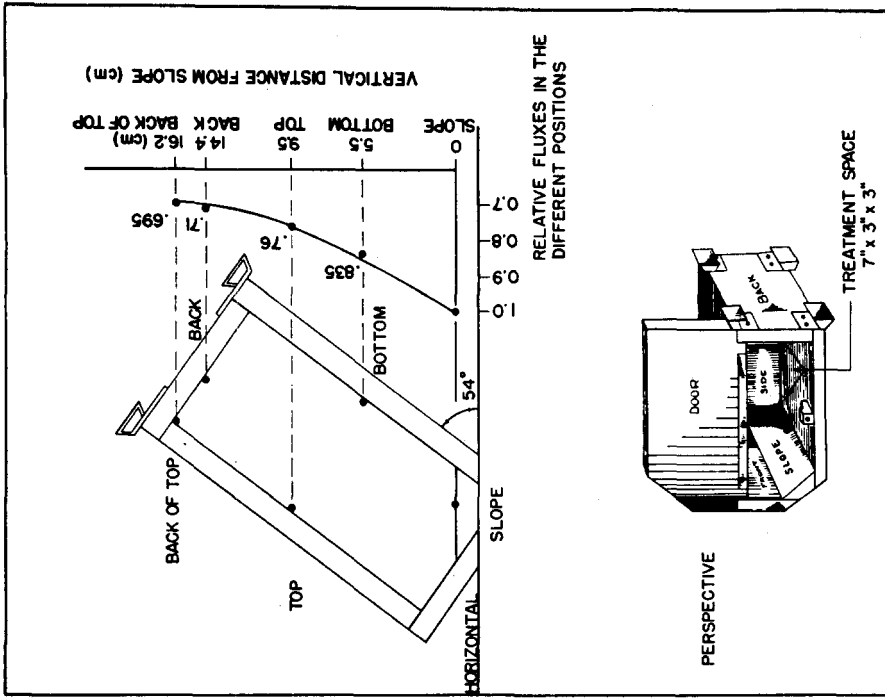


FIGURE 2. Graphite treatment box in the treatment position.

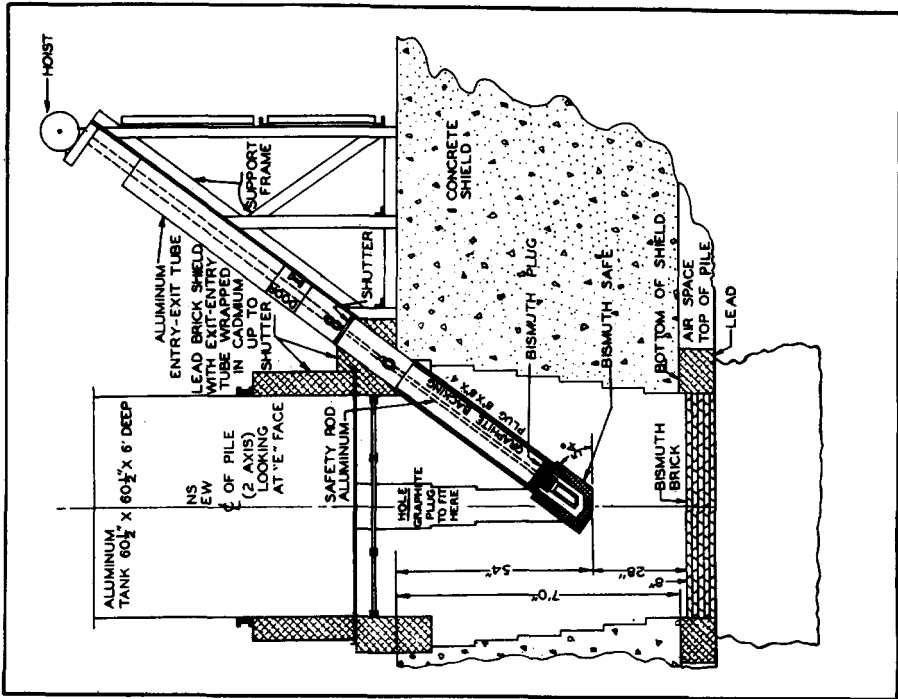


FIGURE 1. Biological thermal neutron treatment chamber.

equal, the number of neutrons captured, and therefore the radioactivity of a sample, is proportional to the number of neutrons incident upon the sample, i.e., the flux. The induced radioactivity of the sample can now be measured on an ionization instrument, and this radioactivity measurement is an expression of the flux by which it was activated. The neutron flux was determined from the induced activity in 0.1 cm² indium foils exposed simultaneously and adjacent to the flower buds on the "slope" of the treatment box. Activity of the indium foils was measured as millivolts on a 100 percent geometry ion chamber (JONES and OVERMAN 1948) and from this the neutron intensity, in the arbitrary unit of millivolts of saturated activity per gram of indium, could be determined.² The standard error (S.E.) of these measurements varied from 0.5 to 2 percent of the mean value.

Conversion of the arbitrary unit of neutron intensity into the absolute unit, thermal neutrons per cm² per second, was made by three independent methods from:

- 1) a comparison of the activity induced in the indium foils in the Oak Ridge standard pile³ (at a known thermal neutron flux) with the activity induced in the thermal column. All measurements were made on the same ion chamber; the value determined is an average of nine separate foil activations.
- 2) a comparison of the beta activity induced in gold foils in the Oak Ridge thermal column with the activity induced in the same foils exposed to a known thermal neutron flux (by beta-gamma coincidence techniques) in the Argonne National Laboratory pile. These foils were activated and calibrated by DR. AL WATTENBERG of the Argonne Laboratory. All

² The formula used to obtain the intensity is: Saturated activity per gram of foil → millivolts

$$= \frac{\text{count (mv)}}{\text{wt (activation factor)(decay factor)}} = \frac{C}{w(1 - e^{-\lambda t_a})(e^{-\lambda t_d})}$$

λ = decay constant

t_a = time of activation = time of exposure

t_d = time of decay, from removal to measurement

and since

$$\text{Dose} = \text{flux} \times \text{time} = \frac{\text{neutrons}}{\text{cm}^2 \text{ sec}} \times \text{sec} = \frac{\text{neutrons}}{\text{cm}^2}$$

then

$$\text{Dose} = \frac{CK t_a}{w(1 - e^{-\lambda t_a})(e^{-\lambda t_d})}$$

K = Conversion of mv/gm → neutrons/cm² sec

For cases where the time of exposure is small in relation to the half life, the integrated dose as measured by the foil can be calculated directly from:

$$D = \frac{CK}{w(e^{-\lambda t_d})\lambda}$$

³ The standard pile is a large mass of graphite containing a radium-beryllium source of neutrons. The flux of thermal neutrons at various positions in this pile had been calculated by the application of neutron diffusion theory and a knowledge of the Ra-Be source strength.

measurements were made on the same Geiger-Müller beta counter, the value is an average of four different foil activations.

- 3) measurements of the activity induced in cobalt samples made on the ion chamber which had been calibrated for absolute measurement of Co^{60} disintegrations per second; the value is an average of seven activations.

The results of these three methods are given in table 1.

TABLE 1

Determination of absolute thermal neutron flux (n_{th} per cm^2 per sec) on the "slope" of the graphite treatment box in the thermal column. Pile constant at full operating power.

METHOD	THERMAL NEUTRON FLUX (n_{th} per cm^2 per sec)
1. Indium foils, 4 mil, 25 cm^2 . Comparison of standard pile-thermal column activations.	1.09×10^9
2. Gold foils, 4 mil, 1 cm^2 . Comparison of Argonne thermal column—Oak Ridge thermal column.	1.29×10^9
3. Cobalt—wire and Co_3O_4 powder measured against known standards.	1.31×10^9
4. Accepted value.	1.25×10^9

Of the three methods, the largest number of measurements was made on indium foils. The accepted value represents quite well the data presented in the table, and will be used as the flux in all subsequent calculations.

As explained above, the neutron intensity to which the plants were subjected can be expressed accurately (± 2 percent) in the arbitrary unit of millivolts (per gram indium activity at saturation). The conversion of this arbitrary unit to the absolute units of $n_{\text{th}}/\text{cm}^2$ sec is subject to some error and possible revision, so the method of conversion is given here:

a flux of $1.25 \times 10^9 n_{\text{th}}/\text{cm}^2$ sec = 89,650 mv/gm satd. activ. of indium foils measured at the 10^9 resistance on the ion chamber, so

$$1 \text{ mv (at } 10^9 \text{ resist.)} = \frac{1.25 \times 10^9}{89,650 \text{ mv}} = 1.394 \times 10^4 n_{\text{th}}/\text{cm}^2 \text{ sec.}$$

This value has been used in all conversions of millivolts into neutron flux.

A summary of the physical characteristics of the graphite treatment chamber is given in table 2.

From the data in table 2, it can be seen that practically none of the radiation received by a specimen in the treatment box is due to fast neutrons; roughly, only $1/8 \times 10^4$ of the activity induced by this neutron field is due to neutrons with an energy > 0.3 electron volts.

Measurement of the inherent gamma-ray contamination inside the facility has been one of the difficult problems of this experiment, since any device put into the bismuth enclosure to measure gamma radiation itself captures neu-

trons and may emit its own gamma rays. Two different methods of estimating the gamma-ray contamination have been tried.

- 1) Using data on the neutron flux and the gamma-ray intensity at the top of the thermal column, the expected gamma-ray intensity at the position of the bismuth safe would be in the ratio of the fluxes. The attenuation of this gamma-ray intensity in going through the 7.94-cm walls of the bismuth safe has been calculated using the absorption coefficient

TABLE 2

Physical characteristics of the "slope" of the graphite treatment box. Pile constant at full power.

CHARACTERISTIC	VALUE	SOURCE
1. Temperature	room temp.	by air circulation drawn from outside into the pile
2. Size of box, inside dimensions	17.5×7.5×7.5 (cm)	figure 2
3. Neutron flux	1.25×10 ⁹ n _{th} /cm ² per sec	table 1
4. Fast neutron contamination	insignificant	cadmium ratio* of indium foils 8.3×10 ⁴ , av. of 3 meas.
5. Inherent gamma-ray contamination	~6 r/min	see text, and table 9
6. Relative flux at different positions in box	see figure 2	simultaneous activation of 0.1 cm ² indium foils placed at the different positions
7. Flux at different positions on the "slope"	uniform	(same as 6. above)

* cadmium ratio is the ratio of the activities induced in a bare indium foil and in a cadmium covered indium foil, and is roughly equal to:

$$\frac{\text{total activity due to neutrons of all energies}}{\text{activity due to neutrons of } > 0.3 \text{ ev only}} \rightarrow \frac{\text{slow} + \text{fast neutrons}}{\text{fast neutrons}}$$

($\tau + \sigma_a + K$ but not including σ_s) for lead corrected for the ratio of bismuth/lead density. The calculation using the values described shows that with the pile operating at full power, the inherent gamma-ray contamination inside the bismuth safe is ~6 r/minute.

- 2) The second method⁴ was to expose in the safe a Victoreen chamber enclosed in a boron¹⁰ coated aluminum can; the boron transmitted the inherent gamma rays but absorbed nearly all the neutrons, emitting its own 0.38 mev capture gamma rays as a result. The attenuation of gamma ray intensity caused by interposing increasing thicknesses of lead between the Victoreen chamber and the boron gave a compound absorption curve; the extrapolation of the energetic gamma ray curve to the zero ordinate showed the inherent gamma ray level to be ~5 r/minute.

These two estimates of the inherent gamma-ray contamination in the treatment position with the pile operating at full power indicate that it is about 6r/minute or 5 r/minute. The value of 6 r/minute will be accepted as the proper one though it is felt that this is a maximum value and the true value is probably somewhat lower.

⁴ This method was developed and the measurements made by G. E. STAPLETON of this laboratory.

BIOLOGICAL METHODS AND MEASUREMENTS

Inflorescences of a clonal line (Sax no. 5) of *Tradescantia paludosa* Anderson and Woodson were used for all experiments. The plants had been grown in pots for about a year before use. Inflorescences were picked the morning of use, stripped of leaves and bracts and made up into groups of about 12 inflorescences arranged flat so there was no overlap of the buds and held together with a 3–4 mm-wide strip of scotch tape near the butt end of the stems. Each group of inflorescences was carefully positioned so that the buds were lined up on the center of the slope of the treatment box. A 0.1 cm² indium foil was placed on the slope of the box about 0.5–1 cm away from the buds. The flux at different positions on the slope had been checked previously and found to be uniform so that all inflorescences received the same dose of thermal neutrons. The treatment box containing the inflorescences and the foil was run into the thermal column for varying lengths of time and the amount of neutron radiation received determined from the measured activity of the simultaneously exposed indium foil.

Aceto-carmin smears were made of the anthers of the treated inflorescences 22–24 hours and four days after radiation and the frequency of the various types of chromatid and chromosome aberrations scored from the temporary slides. Slides were scored under code numbers to prevent bias in scoring. All scoring of aberrations in these experiments was done by one person to eliminate further any bias or difference there may have been in method of scoring. The terminology of aberration types is that of SAX (1940) for chromosome aberrations and of CATCHESIDE, LEA and THODAY (1946) for chromatid aberrations.

RESULTS

The first series of experiments, numbers 9, 10 and 11, were made to analyze the frequency of chromosome aberrations observed four days after irradiation. The data from these three experiments are presented in table 3. Neutron intensity and neutron dose are given in both arbitrary units (mv) and absolute units (n_{th}/cm^2) as described previously using the conversion factor given. Aberrations are as described above.

The data of table 3 are presented graphically in figure 3 following the subsequent tables. A consideration of these and the subsequent biological results will be made in the discussion.

The time required to produce an appreciable number of chromosomal aberrations proved to be quite long—up to 28 minutes for the longest exposure—and the chromosomal aberrations were therefore being produced at a rather low rate. It has been shown in this material (SAX and SWANSON 1941) that the yield of aberrations from cells irradiated in prophase (and which will be in metaphase of division about 22–24 hours later) is three to three and a half times as great as the yield from cells radiated in the resting stage (which will be in metaphase four to five days later). Accordingly, two experiments (numbers 12 and 13) were made for the analysis of the 22–24-hour chromatid aberrations, the longest exposure requiring only eight minutes; the 22–24-hour chromatid aberrations were therefore being produced at a much higher rate

TABLE 3
Frequency of four-day chromosome aberrations from thermal neutron radiation. (See figure 3.)

EXPERI- MENT	TREAT.	EXPOSURE TIME SEC.	INTENSITY* MV. (AT 10^9 RESISTANCE)	DOSE			ABERRATIONS					
				MV. SEC. (ARBITRARY) $\times 10^{-6}$	$n_{th}/cm^2 \dagger$ (ABSOLUTE) $\times 10^{-11}$	NO. OF BUDS	NO. OF CELLS	FRACTION NORMAL CELLS	EXCHANGES \ddagger NO. PER CELL \pm S.E.	DELETIONS \S NO. PER CELL \pm S.E.		
No. 9 (18 Aug. 1948)	A	290	101,000	29.4	4.10	4	379	0.83	31	0.0818 \pm .0091	39	0.103 \pm .0069
	B	580	101,000 \pm .5%	58.4	8.15	5	311	.73	46	.148 \pm .021	57	.183 \pm .026
	C	1160	78,600 \pm .3%	91.2	12.7	5	474	.59	110	.232 \pm .022	161	.339 \pm .029
No. 10 (3 Sept. 1948)	B	840	97,200 \pm .6%	81.6	11.4	4	710	.54	166	.234 \pm .018	268	.374 \pm .023
	C	1680	96,800 \pm .2%	163	22.7	4	830	.34	416	.502 \pm .022	476	.574 \pm .027
No. 11 (14 Oct. 1948)	A	372	94,500 \pm .4%	35.2	4.91	10	1,666	.77	144	.0864 \pm .007	304	.183 \pm .011
	B	744	93,200 \pm .2%	69.4	9.67	11	1,038	.61	198	.191 \pm .014	328	.316 \pm .018
	C	1116	90,200 \pm .8%	101	14.0	8	513	.47	144	.281 \pm .028	211	.411 \pm .030
	D	1488	89,100 \pm 1.0%	133	18.5	7	543	.35	198	.365 \pm .024	357	.657 \pm .012

* Neutron intensity in arbitrary unit \pm S.E.

\dagger mv. sec. $\times 1.394 \times 10^4 = n_{th}/cm^2$, see text.

\ddagger Exchanges = dicentric + centric rings + 2(tricentric) \pm S.E. (where population size = no. of cells scored)

\S Deletions = terminal + large and small isodiametric (but excluding acentric rings)

than the four-day chromosome aberrations. The data from experiments 12 and 13 are given in table 4, and these results are presented graphically in figure 4.

An X-ray experiment was made to compare with the results of aberration analysis from thermal neutron experiments 12 and 13. Since it was desired

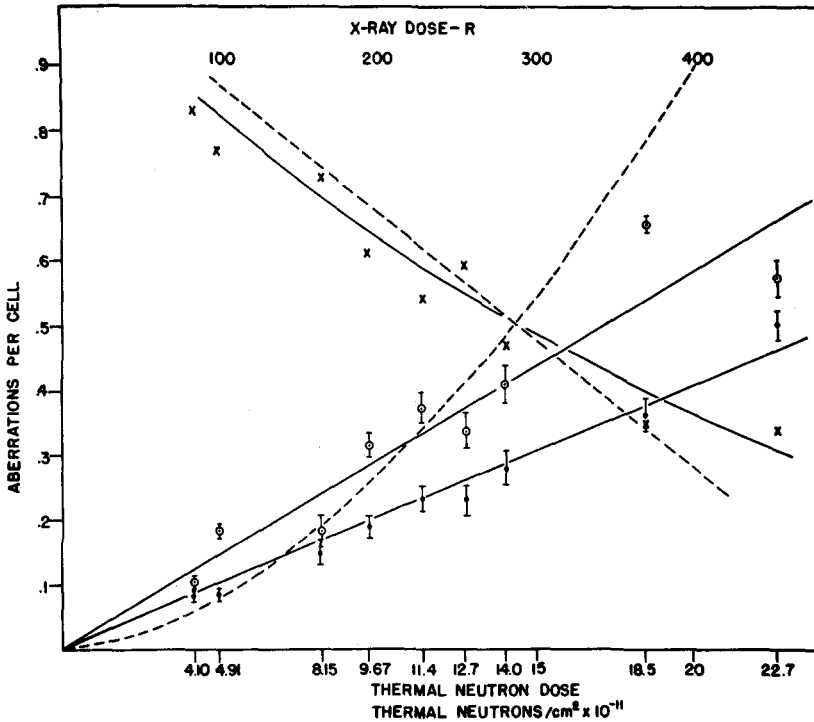


FIGURE 3. Yield of four-day chromosome aberrations from thermal neutron radiation. Data in table 3.

— Thermal neutrons
 - - - X-rays

- chromosome exchanges = dicentrics + centric rings + 2(tricentrics)
- chromosome deletions = terminal + large and small isodiametrics
- × fraction of normal cells = no aberrations

Lines drawn are the least squares fit to the data.

Curves for the chromosome exchanges and fractions of normal cells resulting from X-radiation (average 50 r/min) are superimposed for comparison.

X-ray curves were made from data taken from: SAX, K. 1948, Oak Ridge Information Meetings; MARINELLI, NEBEL *et al.*, 1942. *Amer. J. Bot.* 29: 866-874; GILES, N. H., JR. and H. P. RILEY, 1949. *Proc. Nat. Acad. Sci.* 35: 640-646.

that the thermal neutron and X-ray exposures be given at approximately the same intensity, X-rays were given at a rate calculated to produce the same number of aberrations in the same exposure time. X-rays were given at 250 kv peak, 15 ma with inherent filtration equivalent to 3 mm Al and added filters 1/2 mm Cu and 1 mm Al. Dose was measured with a Victoreen chamber calibrated sometime previously by the Bureau of Standards. Measurements

TABLE 4
Frequency of 22-24-hour chromatid aberrations from thermal neutron radiation. (See figure 4.)

EXPERI- MENT	TREAT.	EXPOSURE TIME SEC.	INTENSITY MV. (AT 10 ⁹ RESISTANCE)	DOSE			ABERRATIONS							
				MV. SEC. (ARBI- TRARY) X 10 ⁻⁶	RH ₀ /CM ² (ABSO- LUTE)	NO. OF BUDS	FRACTION CHROMA. NORMAL DELET. CELLS	ISOCROMATID DELETIONS		CHROMATID+ ISOCROMATID		EXCHANGES*		
								NO.	PER CELL ± S.E.	NO.	PER CELL ± S.E.	NO.	PER CELL ± S.E.	NO.
No. 12 (9 Dec. 1948)	A	120	95,000 ± 3%	11.4	1.59	9	0.58	190	132	0.185 ± .017	322	0.452 ± .027	53	0.074 ± .011
	B	240	93,300 ± 1.6%	22.4	3.12	3	.35	161	177	.442 ± .033	338	.843 ± .046	61	.152 ± .021
	C	480	97,600 ± .5%	46.9	6.53	5	.14	470	452	.679 ± .032	922	1.39 ± .045	200	.301 ± .023
No. 13 (12 Jan. 1949)	A	180	92,400 ± 3.6%	16.6	2.32	5	.48	171	99	.236 ± .025	270	.658 ± .036	39	.093 ± .015
	B	360	93,800 ± .6%	33.8	4.71	4	.28	162	139	.463 ± .035	301	1.00 ± .037	51	.170 ± .025

* Exchanges = c/c symmetrical + asymmetrical interchanges (CATCHESIDE).
= chromatid dicentric + exchanges (SAX).

TABLE 5
Frequency of 22-24-hour chromatid aberrations from X radiation. Average intensity, 17 r/min.
250 kv peak, 15 ma; equiv. 3 mm. Al. inherent, added 1/3 mm Cu, 1 mm Al.

EXPERI- MENT	TREAT.	EX- POSURE TIME (sec.)	IN- TENSITY r/min.	DOSE r	NO. OF BUDS	NO. OF CELLS	FRACTION NORMAL CELLS	ABERRATIONS						
								CHROMA. DELET.	ISOCROMATID DELETIONS	CHROMATID+ ISOCROMATID	EXCHANGES			
											NO.	PER CELL ± S.E.	NO.	PER CELL ± S.E.
X Ray	A	86	17.6	25.2	3	795	0.78	141	50	.0629 ± 0.0088	191	.240 ± .017	13	.0163 ± .0045
No. 14 (24 Jan. 1949)	B	172	17.6	50.4	3	450	.62	126	58	.129 ± .013	184	.409 ± .032	24	.0533 ± .011
	C	344	16.1	92.2	6	400	.40	191	135	.338 ± .030	326	.815 ± .062	49	.123 ± .018
	D	585	16.3	159	4	260	.10	291	170	.654 ± .044	461	1.77 ± .069	69	.266 ± .033

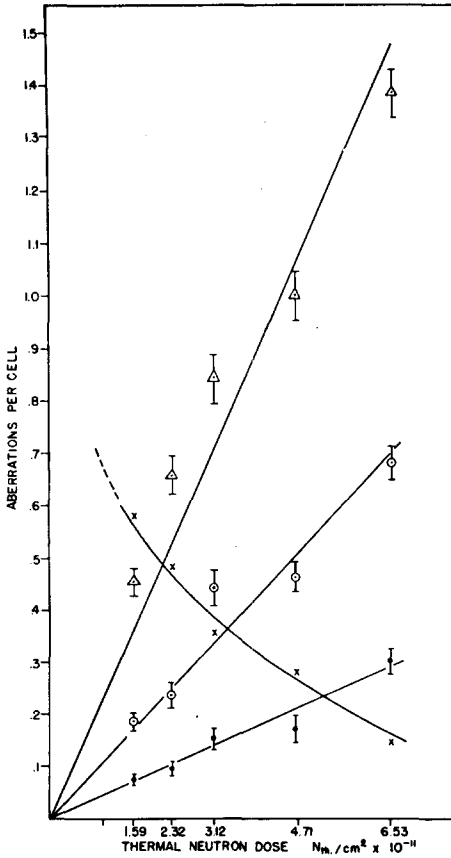


FIGURE 4. Yield of 22-24-hour chromatid aberrations from thermal neutron radiation. Data in table 4.

- chromatin exchanges = c/c interchanges
- isochromatid deletions
- △ chromatin + isochromatid deletions
- × fraction of normal cells = no aberrations

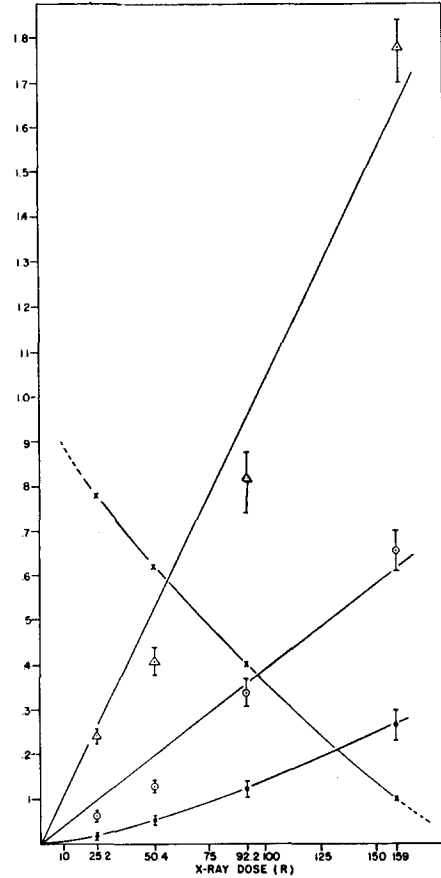


FIGURE 5. Yield of 22-24-hour chromatid aberrations from X-radiation. Average 17 r/min. Data in table 5.

- chromatin exchanges = c/c interchanges
- isochromatid deletions
- △ chromatin + isochromatid deletions
- × fraction of normal cells = no aberrations

were made before, during and after each treatment of inflorescences. Absolute exposures may be in error by \pm five percent, relative exposures are more accurate. The data of the X-ray experiment, X-14 are given in table 5, these results graphically in figure 5.

DISCUSSION

Before we can discuss the results just presented, we must consider the radiations to which the material has been exposed. The ionization produced in the Tradescantia tissue in the present experimental device can be analyzed into the following components:

- 1) Contamination:
 - a) fast neutron contamination

- b) inherent gamma-ray contamination
- 2) From thermal neutron capture reactions in the inflorescences:
 - a) from immediate "capture" radiations, of which the most important are due to:
 - 1) hydrogen
 - 2) nitrogen
 - 3) boron
 - b) from subsequent radioactive decay from the radioactive isotopes formed.

These components of the ionization dose will be considered in order. The levels of inherent fast neutron contamination (zero) and gamma-ray contamination (about 6 r/minute, max.) have been indicated already in table 2.

Let us consider the kinds and amounts of ionizing radiations produced by thermal neutron capture reactions. Since these reactions are ones of capture by the atoms of the elements present in the tissue, the kinds of ionizing radiations emitted will depend on the emission reactions of the elements, which are known; the amount emitted by any element, and the amount absorbed in the tissue will depend on the values of the following characteristics:

Ionization energy per unit volume of tissue per unit time =

$$F \times N \times \sigma \times E \times A \quad (1)$$

where:

- 1) F = thermal neutron flux = number of neutrons crossing a square centimeter per second, which is the same for all elements.
= $n_{th}/\text{cm}^2 \text{ sec}$

- 2) N = the number of atoms of an element per unit volume of tissue

$$= \frac{\% \text{ of wt.} \times 0.602 \times 10^{24}}{100 \times \text{at. wt.}} = \text{atoms/cc. Density} = 1$$

- 3) σ = capture cross section of an element for thermal neutrons, which is the area in cm^2 that a single nucleus of an element presents to a beam of incident neutrons.

$$= \text{value in "barns"} \times 10^{-24} \text{ cm}^2$$

- 4) E = energy of the radiation(s) emitted by the element after a neutron is captured.

$$= \text{mev (million electron volts)}$$

- 5) A = the fraction of this energy E emitted per reaction which is absorbed in the tissue; this depends on the type of radiation (α , β , or γ), its absorption coefficient in the tissue, and the thickness of tissue to be traversed.

$$= 1 - e^{-\mu t G} \text{ where:}$$

$$\mu = \text{abs. coeff. in cm}^{-1} \text{ for the radiation in tissue}$$

$$t = \text{thickness of tissue, cm}$$

$$= .16 \text{ cm, radius of the whorl of six anthers}$$

$$G = \text{geometry correction for radiations losing only a small fraction}$$

of their energy in the tissue; it decreases the thickness of tissue traversed by the factor 0.75, as will be explained later.

Expressing all the values of equation (1) in the proper units and using the proper conversion values of mev into roentgen-equivalent-physical (rep), a good estimate of the amount of ionization produced in a given volume of tissue by any element for a given flux of thermal neutrons will be:

$$\text{rep per minute} = \frac{(F \times 60)N\sigma(E \times 10^6)A}{5.22 \times 10^{13}} \quad (2)$$

where 1 r = 83 ergs/gm tissue

$$1 \text{ e.v.} = 1.59 \times 10^{-12} \text{ ergs}$$

hence

$$1 \text{ r} = \frac{83}{1.59 \times 10^{-12}} = 5.22 \times 10^{13} \text{ e.v.}$$

Calculations of the rep/minute due to each of the elements present in the Tradescantia tissue have been made using equation (2); the results are given

TABLE 6

rep/minute of ionization absorbed in Tradescantia tissue due to capture reactions of each of the elements present. Constant flux of 1.25×10^8 n_{th}/cm^2 per sec. Discussion in text; see Equation (2).

ELE- MENT	ATOMIC WEIGHT	PERCENT* OF WET WEIGHT	N NO. OF ATOMS PER CC. $\times 10^{24}$	σ CAPTURE CROSS SECTION $\times 10^{24}$ cm ²	E CAPTURE RADIA- TION EMITTED AND ENERGY		A FRACTION OF ENERGY ABSORBED IN TISSUE	REP./MIN. ABSORBED IN TISSUE	PERCENT OF TOTAL REP./MIN.
					TYPE	ENERGY (mev)			
H	1.008	10.5	.062,6	0.32	γ	2.23	.003,1	0.194	16.0
B	10.82	.000,287	.000,000,16	715.	α^{++}	2.40	1.0	.394	32.3
C	12.01	6.45	.003,23	.004,5	γ	5.0	.002,6	.000,28	.02
N	14.008	.997	.004,29	1.7	p^+	0.6	1.0	.628	51.5
O	16.00	81.3	.030,6	<.001	γ	>2	.003,1	.000,27	.02
Na	22.997	.100	.000,026	.45	γ	>1	.003,9	.000,07	.005
Mg	24.32	.040	.000,009,9	.3	γ	>1	.003,9	.000,017	.001
P	30.98	.127	.000,024,7	.23	γ	>1	.003,9	.000,32	.03
S	32.06	.066	.000,012,4	.4	γ	>1	.003,9	.000,028	.002
Cl	35.457	.032	.000,005,44	40.	γ	>2.8	.003,2	.000,28	.02
K	39.096	.35	.000,053,9	2.5	γ	>1	.003,9	.000,75	.06
Ca	40.08	.01	.001,001,5	.5	γ	>1	.003,9	.000,004	.000,3

* Chemical analysis: H, C, N, O, P, S, Cl
Spectrographic analysis B=2.87 \pm .06 ppm.
LEA, '47, page 7, Na, Mg, Ca, K

in table 6. Table 6 shows that hydrogen, nitrogen, and boron reactions account for 99 percent of all the ionization produced in the tissue by neutron capture, and that the ionization produced by all the other elements combined is insignificant.

The chemical composition of the tissue was determined from anther samples taken from the same plants and from buds at about the same stage as those

irradiated. The major elements were analyzed for chemically⁵ from a sample of ~1,200 anthers. A second sample (~2,200 anthers) was analyzed spectrographically for the minor elements,⁶ since some of these might be important in capture reactions because of their extremely high cross sections; examples are cadmium, gadolinium, etc. The spectrographic analysis, shown in table 7, demonstrated that all the minor elements, except boron, could be ignored in these considerations.

Capture cross sections are from WAY and HAINES (1948) and are the most recent and best values.

TABLE 7

*Spectrographic analysis of Tradescantia anther ash. 2.2-gm sample, ~2,200 anthers.
(For chemical analysis, see table 6.)*

ANALYSIS	ELEMENTS
Very strong	Ca
Strong	Mg
Moderate	Al, Fe, K, Mn, P
Weak	Cr, Na, Si
Very weak	Cu
Trace	Ni
Faint trace	B(2.87 ± .06 p.p.m. wet wt.) Mo, Pb, Sn, Ti?
Very faint trace	Ag
Sought, not found	As, Au, Ba, Bi, Cd, Co, Dy, Er, Eu, Gd, Ge, Hf, Ho, In, Ir, La, Li, Lu, Nd, Pr, Pt, Rb, Re, Rh, Ru, Sb, Sc, Sm, Sr, Tb, Tm, V, Y, Yb, Zr

The values for the radiation emitted and its energy are taken from various sources in the literature. The radiations in table 6 are only the "capture" emissions from the compound nucleus, and are emitted almost instantaneously after capture; the radiations emitted subsequently by whatever radioactive daughter elements that may be formed are not considered.

The fraction of the energy emitted which is absorbed in the tissue is important only in the case of gamma-ray emission, since the paths of the 0.63-mev nitrogen proton and the 2.4-mev boron alpha particle are so short in tissue (~10 μ for the proton and ~13.5 μ for the alpha particle) that all the energy of these particles will be absorbed as ionization produced within the tissue. Only a very small fraction of the gamma rays' energy will be expended in producing ionization within the tissue however, and this fraction can be estimated as has been shown.

A geometry correction (0.75) of the loss of gamma-ray energy is necessary because the gamma rays can originate anywhere on a radius of the whorl of anthers in the bud but will have a biological effect only by the ionization produced within the anthers. An integration of the distribution of reactions shows that the average gamma ray will traverse 0.75 times the radius of the whorl of anthers.

⁵ The quantitative analysis was made by the OAKWOLD LABORATORIES, Alexandria, Virginia.

⁶ The spectrographic analysis was made by CYRUS FELDMAN of this laboratory.

The last source of ionization within the tissue, that due to the induced radioactivity from neutron capture, is still to be considered. Hydrogen and boron, which account for most of the capture processes in tissue, have no subsequent radioactivity and can be ignored. Considering all the elements present in the tissue and using the values for percent of wet weight and the cross sections, it was calculated that of all the capture reactions that occurred in the tissue, hydrogen accounted for 72 percent, nitrogen for 26 percent, chlorine for 0.8 percent, boron for 0.4 percent and potassium for about 0.5 percent; no other element accounted for as much as 0.1 percent. It can be shown from the data in table 6 and from other considerations of half life and types of radiations emitted that the only element which could contribute appreciably to the total ionization dose absorbed by reason of its radioactive decay is chlorine³⁸. Chlorine³⁸ decay is as follows:

$$\beta^- 4.9 \text{ mev (53\%)}, \quad 2.8 \text{ mev (11\%)}, \quad 1.2 \text{ mev (36\%)}$$

$$\gamma 1.60 \text{ mev}, \quad 2.15 \text{ mev.}$$

and the total amount of absorbed ionization due to chlorine decay can be estimated as has been done previously for the other elements. The greatest uncertainty exists in the estimate of the fraction of the beta ray energy absorbed, in which conditions of geometry, chlorine distribution and other factors can lead to considerable differences in the result. Using two different methods of

TABLE 8

Components of the ionization dose absorbed in 1 gram (1 cc) of Tradescantia tissue, at constant flux of 1.25×10^9 n_{th}/cm^2 sec. Data from previous tables and calculation.

SOURCE OF COMPONENT	TYPE OF RADIATION	rep/MIN	rep PER 1×10^{11} n_{th}/cm^2	PERCENT OF TOTAL rep	PERCENT OF CAPTURE rep
(1) Fast neutron contamination	p^+ recoil	negligible	negligible	—	—
(2) Inherent gamma-ray contamination	γ	6.0 r max.	8.0	82	—
Capture processes					
(3) H capture	γ	0.195	.260	2.7	15
(4) N capture	p^+	.628	.837	8.6	48
(5) B capture	α^{++}	.394	.525	5.4	29
(6) Induced radioactivity (from Cl ³⁸)	β^-, γ	$\sim .100$ (.52 max)	.133 (.69 max)	1.4	7.5
Subtotals:					
all capture:					
H+N+B+Cl	$\gamma + p^+ + \alpha^{++} + \beta^- + \gamma$	—	1.75	18.0	—
from N+B only	$p^+ + \alpha^{++}$	—	1.36	14	78
Total:					
γ contam. + capture	$\gamma, + \gamma + p^+ + \alpha^{++} + \beta^- + \gamma$	—	9.75		

estimate, the limits of the total ionization absorbed from chlorine³⁸ decay ($\beta^- + \gamma$) is ~ 0.10 rep/minute, but could extend up to a maximum of 0.52 rep/minute. To check on the induced radioactivity, a sample of buds was counted for four hours after removal from a 30 minute exposure and found to decay with a 37 minute half life, corresponding to the decay of chlorine³⁸. The C^{14*} 0.15 mev beta ray could not be detected by the method used, but at worst could amount to only 0.003 rep in two days, an insignificant amount. We conclude that the contribution to the ionization dose from radioactive decay is small and is almost entirely due to the decay of chlorine³⁸.

Using all the data which have been presented previously, it is now possible to express the sources and amounts of the ionization energy which are expended in the *Tradescantia* tissue; this is done in table 8. The unit of dose is $1 \times 10^{11} n_{th}/cm^2$ as this is the unit dose in the biological experiments. It is seen that the gamma ray contamination makes up a large share of the rep absorbed; these are physical values, however, and do not involve the relative biological efficiencies of the various types of radiations, which will be considered later.

Thermal neutron and X-ray biological equivalence and efficiencies: The data given in the section on biological results are a quantitative measure of the identical response produced by thermal neutrons and X-rays. All possible care was exercised to be sure that the only difference between the X-ray and thermal neutron experiments was the radiation itself. Therefore, the dose of radiation, X-ray and thermal neutron, required to produce the same amount of effect is a measure of the biological equivalence of thermal neutrons to X-rays. This neutron/X-ray comparison has been made for three classes of aberrations: isochromatid deletions, chromatid plus isochromatid deletions, and fraction of normal cells; the equivalence based on isochromatid deletions is probably the most accurate one, since these aberrations can be observed more accurately than the other types. These "one-hit" aberrations can be compared because it has been repeatedly demonstrated (LEA 1947; KOTVAL and GRAY 1947) that they vary linearly with dose for all radiations, X, gamma, and heavy particles (the same is not true for the exchange or "two-hit" aberrations).

A correction must be made in the thermal neutron experiments for the fact that a certain proportion of the ionization dose is due to the inherent gamma-ray contamination of the facility and is not due to thermal neutrons at all (table 8); the same correction applies to the amount of biological effect observed, which is due to thermal neutrons plus inherent gamma-ray contamination (figs. 3 and 4). The correction has been made by subtracting from the total effect due to neutrons plus gamma rays, the amount of effect due to that dose of gamma rays ($8r$) associated with a unit dose of thermal neutrons ($1 \times 10^{11}/cm^2$), as follows:

$$E_{n \text{ alone}} = (E_{n+\gamma}) - E_{\gamma}$$

where:

E_n = effect due to dose D_n of neutrons

E_{γ} = effect due to dose D_{γ} of gamma rays associated with D_n of neutrons

$E_{n+\gamma}$ = effect due to $D_n + D_{\gamma}$.

TABLE 9
Biological equivalence and efficiency of thermal neutrons/X rays. Data from previous tables and figures.

BIOLOGICAL EFFECT	COEFFICIENT OF PRODUCTION PER CELL = C			BIOLOGICAL EQUIVALENCE†		DAILY "TOLERANCE DOSE" 8 HOURS	REF. § FROM 1 X 10 ¹¹ n _{th} /cm ²	BIOLOGICAL EFFICIENCY	
	n _{th} + γ CONTAM.*	CORRECTED‡ n _{th} ALONE	X-RAYS* X-RAYS*	1 r OF X-RAYS EQUALS	1 X 10 ¹¹ n _{th} /cm ² EQUALS			OF D _{th} TO X-RAYS (H _γ + N _p + B _α + C _{β-γ})	OF p ⁺ + α ⁺⁺ TO X-RAYS (N _p + B _α + C _{β-γ})
Isochromatid Deletions	0.1070 X 10 ⁻¹¹	0.07598 X 10 ⁻¹¹	0.003878	5.10 X 10 ⁸ n _{th} /cm ²	19.59 r	5.1 X 10 ⁸	1.75	11.2/1	14.1/1
Chromatid + Isochromatid Deletions	0.2257 X 10 ⁻¹¹	0.1426 X 10 ⁻¹¹	0.01039	7.29 X 10 ⁸	13.73 r	7.3 X 10 ⁸	1.75	7.8/1	10.8/1
Chromatid Exchanges	0.04425 X 10 ⁻¹¹	—	0.002416 (R) ^{1,5}	—	—	—	—	—	—
Chromatid 50% Normal Cells Dose	2.05 X 10 ⁻¹¹	—	(72r - 16.4γ contam.) = 55.6 r	3.69 X 10 ⁸	27.12 r	3.7 X 10 ⁸	1.75	15.5/1	19.9/1
Chromosome 50% Normal Cells Dose	14.5 X 10 ⁻¹¹	—	(290 r - 116γ contam.) = 174 r	8.33 X 10 ⁸	12.00 r	8.3 X 10 ⁸	1.75	6.9/1	8.8/1
Chromosome Exchanges	0.02069 X 10 ⁻¹¹	—	0.0149 (R) ^{1,7b}	—	—	—	—	—	—
Best Value	—	—	—	~5 X 10 ⁸ n _{th} /cm ²	~20 r	~5 X 10 ⁸	—	~11/1	~15/1

* See graphs, figs. 3, 4, 5.
† See text for correction for γ contamination.

‡ Equivalence = $\frac{C_{n\text{th}}}{C_{X\text{-rays}}}$

§ See table 8.

|| Efficiency = $\frac{\text{observed X-ray equiv. effect}}{\text{calculated rep.}}$

Tolerance Flux = $\frac{5 \times 10^8}{8 \times 60 \times 60} = 17,360$ n_{th}/cm² per sec.

Such a correction for gamma rays is possible because it has been shown that unit doses of X- and gamma rays produce almost the same amount of these aberrations (KOTVAL, in LEA 1947, p. 239).

The equivalence of thermal neutrons to X-rays has been obtained by comparing the corrected thermal neutron effect with the X-ray effect for the same aberrations. The results of these comparisons are given in table 9.

If we assume the standard value for daily tolerance dosage, 0.1 r of X-rays per eight-hour day, to be that amount of any radiation producing an effect equal to this dose of X-rays, then the "tolerance dose" of thermal neutrons based on this biological effect is as shown in table 9.

We can in addition obtain an efficiency of thermal neutrons and X-rays in producing this biological effect by comparing the X-ray equivalent effect with the calculated amount of rep generated by a unit dose of thermal neutrons. This comparison has been made in the last two columns of table 9.

The observed biological efficiencies could be explained solely by errors involved in the estimate of the ionization dose absorbed in the tissue. This possibility has been considered but it is believed that the observed efficiency ($\sim 11/1$) is too great to be accounted for by such errors, for the following reasons: the gamma ray contamination would have to be two and one-half times as great as estimated, the rep generated by thermal neutron capture six and one-half times as great, and the rep due to radioactive decay 80 times as great. Errors in the estimate of dose undoubtedly exist, but it is very unlikely that the estimated dose is wrong by two and one-half to six and one-half times, and therefore the efficiency observed is to be explained by other reasons, which will now be considered.

The comparison made in the last two columns of table 9 assumes that the inherent gamma-ray contamination has the same effect per unit dose as X-rays; further, the same is probably true for the hydrogen gamma rays and the chlorine³⁸ beta and gamma rays, since they occur at random in the cells. This leaves us with the nitrogen protons and the boron alpha particles to consider, and apparently the combined $p^+ + \alpha^{++}$ radiation has an efficiency to X-rays per unit of ionization of about 15/1 (last column, table 9). There are two lines of reasoning for believing that the protons plus alpha rays must indeed have this high efficiency in producing chromosomal aberrations. The first is the comparison of the amount of X-ray equivalent effect produced by a given dose of thermal neutrons with the calculated number of rep produced by the same dose. The second is based on the well established fact that the yield of the exchange or "two-hit" aberrations varies as a power (greater than 1) of the dose for X- and gamma rays, but linearly with dose for protons and alpha rays. If, indeed, the major part of the effect in this experiment is due to gamma radiation, which comprises 85 percent of all the ionization received by the tissue (table 8), we would expect that this preponderance of gamma radiation would be reflected in the exchange or "two-hit" aberration curve increasing more rapidly than the first power of the dose. On the contrary, it can be seen in the two thermal neutron graphs (figs. 3 and 4) that the frequencies of the chromosome and chromatid exchanges increase linearly with dose, but as the 1.5 power of the dose for the comparable X-ray

exposure (figure 5). Apparently the major part of the effect is produced by a radiation of heavy particles, as is concluded from the physical calculations.

The combined efficiency of the nitrogen protons and boron alpha rays must be about 15 times as great as X-radiation for the neutron dose to produce an effect equal to the observed X-ray equivalent dose. KOTVAL and GRAY (1948) have determined the efficiency of protons (from fast neutron recoils) and radon alpha particles to hard X-rays in producing the same aberrations in *Tradescantia* as are analyzed here. A comparison of the efficiency from external sources with their efficiency when originating internally from neutron capture shows:

RADIATION	EFFICIENCY TO X RAYS IN PRODUCING:	
	ISOCHROMATID DELETIONS	CHROMATID PLUS ISOC.D.
1) From external sources:		
protons	3.7/1	2.6/1
alpha particles	7.8/1	4.1/1
expected from a beam of 62% p+38% α	5.2/1	3.2/1
2) Observed from thermal neutron beam of 62% p+38% α	14/1	11/1
3) Ratio: obs/expect.	2.7/1	3.4/1

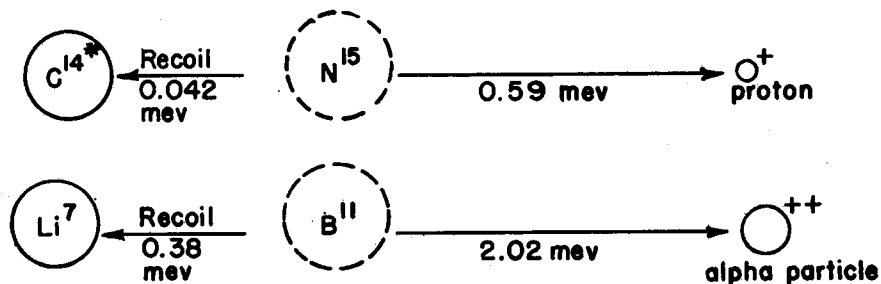
and it is clear that alpha particles and protons are more efficient when originating internally than when they come from external sources.⁷

This large and unexpected biological efficiency of protons and alpha rays resulting from thermal neutron capture, when compared with the efficiency of protons and alpha rays from external sources, suggests that there may be something which has been previously unconsidered or some difference between a biological reaction when the radiation enters the cell from without, and when it originates within the cell. Several mechanisms suggest themselves to account for this difference. It may be that the internal radiations cause chromosome breakage by indirect, in addition to direct, methods; this seems unlikely, however, since once emitted the particles behave the same as those coming from outside the cell. There is, however, one apparently important difference between particles coming from without the cell and those originating internally from thermal neutron capture. Particles coming from external sources

⁷ The energies of the protons being compared are roughly about the same, 0.6 mev from nitrogen captures, and a spectrum of proton energies from the Li-D neutrons with 50 percent of the protons in the 0-1 mev range, 19 percent 1-2 mev 12 percent 2-3 mev, 4 percent 3-4 mev, etc. The α energies are quite different, 2.40 mev from boron captures, 5.49 from radon. The ion densities in tissue are about 2/1 ($\sim 2,500$ ions/ μ for boron α 's, $\sim 1,200$ ions/ μ for radon α 's), but in any case both of these α 's have ion densities far in excess of the value generally accepted, ~ 200 ions/ μ , as the density necessary for the probability of chromosomal break to approach unity. The observed p⁺ and α^{++} efficiencies are therefore probably not to be explained by these energy differences.

are distributed at random in the cell, but the particles originating from neutron capture are distributed as are the nitrogen and boron. Now, the frequency of chromosome breaks is dependent on the ratio of the target volume (the chromosomes) to the number of particles traversing the area; and if the concentration of nitrogen and boron per unit volume is greater in the nucleus and the chromosomes than the rest of the cell then the particles are not distributed at random and the number of "hits" on the chromosomes would be greater per unit dose than from randomly distributed protons and alpha particles. No definite data are available regarding the intracellular distribution of nitrogen, but apparently it is not unusually concentrated in the nucleus as a whole in rat liver cells (SCHNEIDER 1948) though it may be concentrated somewhat in the chromosomes. It seems likely that the boron may in fact be considerably more concentrated in the nucleus and chromosomes than in the cytoplasm, as observations of microincinerated resting stage cells have shown the bulk of the inorganic salts is concentrated in the nucleus with only small amounts thinly and evenly distributed in the cytoplasm (HORNING 1941). The constituents of these nuclear ashes have not been completely analyzed, but it seems reasonable that boron may be among them and is therefore more concentrated in the nucleus. Since the range of these 2.4 mev boron alpha particles is only 13 microns in tissue, and the diameter of the nucleus at the time these cells are exposed to radiation is about 12 microns,⁸ there would be more particulate ionization in the nucleus than the rest of the cell. In addition, if a nitrogen or boron capture reaction occurs in a chromosome, the probability that either the particle or its recoil atom will traverse the chromosome and cause a break can be expected to be unity.

There exist two other likely explanations for the greater efficiency of internal to external originating protons and alpha particles, which are the recoil of the emitting atoms, and the transmutation of the emitting atoms. Let us consider the effect of the recoil atoms from the nitrogen and boron reactions. For both of these, the total energy of the reaction is divided between the particle and the emitting atom, so that the atom itself has energy and will recoil as is diagrammed below:



⁸ Measurements have been made of the dimensions of the microspores used for these experiments. Cells have been selected which were at about the stage of development at which cells would be at the time of radiation—i.e., about four days before metaphase. About 100 cells were measured, from five different buds. Dimensions are as below (in microns):

Cells, outside dimensions: 32.1 long, 21.2 wide. Nucleus: 11.6 diam. Chromosomes (six, haploid): diam. 0.1, length 490. Chromosome dimensions are from SAX and SAX (1935).

Little is known about the range of these heavy recoil atoms, but certainly the energy is sufficient to break chemical bonds, and very likely is enough to break chromosomes. There is a likelihood that the dense ionization of the recoil atoms may increase chromosome aberration yield by injuring broken ends excessively so that the usual X-ray or neutron probability of chromosomal restitution is decreased; this seems to be true for alpha particles applied externally (KOTVAL and GRAY 1947).

Returning to the nitrogen and boron reactions given above, we see that whenever a capture reaction occurs, not only is a particle emitted and the atom recoiled out of position, but a new element is formed *in situ*, carbon from nitrogen and lithium from boron. This may be disastrous, particularly in the case of nitrogen which is an integral part of the protein molecules of the chromosome. The transformation of a nitrogen atom in a protein molecule into carbon may completely disrupt the molecule and possibly neighboring molecules. Almost nothing is known about the incorporation of boron in the cell, but it seems less likely that it is an integral part of the molecules of the chromosome.

Of the explanations given above for the differences of efficiency between external and internal particulate radiation, probably the most valid ones are the increased number of chromosome "hits" per unit dose because in the case of boron the emitting atoms are more concentrated in the nucleus and the chromosomes than in the cytoplasm; the recoil of the emitting atoms; the increase in the probability of a break by a traverse to unity; and the decrease of restitution probability by excessive injuring of broken ends by recoil atoms or alpha rays. The mere act of transmutation of an element in a chromosome seems to be an unlikely cause of chromosome breakage, though it may well account for gene mutation.

The daily "tolerance dose" and "tolerance flux" given in table 9 is understood to apply only to the production of this specific effect, chromosome aberrations, in a specific organism, *Tradescantia*. The temptation exists to apply the tolerance dose so derived to mammals and particularly to man but the physical and biological differences of the two cases make caution necessary in such a comparison. However, this study does demonstrate that there are several important factors which have not been considered in previous calculations of the tolerance dose and flux of thermal neutrons.⁹ The first is the considerable contribution to the dose made by boron, which in this case is 29 percent of the total ionization dose due to capture alone. The second is that particulate radiation originating internally by neutron capture has an unusually high and unexpected efficiency in causing this biological damage, and is about three to three and a half times as damaging as the same dose of particulate radiation applied from without the cell.

⁹ The apparent agreement between the tolerance flux of thermal neutrons derived from these experiments on *Tradescantia* and from the theoretical calculations of a tolerance flux for man derived by MITCHELL (1947) (tolerance flux Mitchell $1.24 \times 10^4 n_{th}/cm^2$ sec; this experiment = 1.74×10^4) is purely fortuitous. The theoretical considerations of physical characteristics made by MITCHELL differ from the situation in the present experiment by numerous features.

SUMMARY

The cytogenetic effect of thermal neutrons from a special facility in the thermal column of the Oak Ridge nuclear reactor has been investigated. The production of chromosomal aberrations, both chromatid and chromosome types, in *Tradescantia* microspores has been compared with the production of the same aberrations by X-rays. Calculations of the number of roentgen equivalent physical absorbed from thermal neutron capture in tissue indicate that three elements, hydrogen, nitrogen and boron are responsible for about 99 percent of the ionization dose produced by neutron capture, and that about 77 percent of this dose is due to the protons and alpha rays from nitrogen and boron capture reactions. These conclusions are substantiated biologically by the observed linear increase of exchange aberrations with dose, which is characteristic of particulate radiation (with electromagnetic radiation, exchange aberrations increase as a power of the dose).

An equivalence of thermal neutrons/X-rays has been derived by comparing the production of chromosomal aberrations by the two radiations. The best value seems to be $\sim 5 \times 10^9$ thermal neutrons per $\text{cm}^2 = 1$ r of X-rays in biological effect; this would make the eight-hour tolerance dose (the same amount of effect as 0.1 r of X-rays) as based on this effect $\sim 5 \times 10^8$ thermal neutrons per cm^2 .

A comparison of the X-ray equivalent effect produced by unit dose of thermal neutrons with the calculated number of roentgen equivalent physical generated by the same dose shows that thermal neutrons are about eleven times as efficient as X-rays per unit dose in producing this biological effect. If only the nitrogen protons and boron alpha rays from thermal neutron capture are considered, their efficiency compared with X-rays seems to be about 15/1. These biological efficiencies are about three to four times as great as have been observed when the same types of radiations were delivered from external sources. It is believed that this difference in the effectiveness of protons and alpha rays when they are administered to a tissue from an external source and these same radiations when they originate from the atoms of the tissue itself is not due to any difference in the effect of the protons and alpha rays themselves, but is due to a difference in their place and manner of origin.

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