auteurs montrent que le PEA est inhibiteur de la réaction d'acétylation du sulfamide, que le CoA reverse cette inhibition, qui est du type non compétitif pour l'acétate.

G. MILHAUD et J.-P. AUBERT

Laboratoires des Isotopes, Institut Pasteur, Paris, le 2 décembre 1955.

Summary

In tissues of higher animals the two principal reactions which lead to the formation of active acetyl are inhibited by phenylbutyrate and phenylvalerate. The non competitive nature of the inhibition is important from the chemotherapeutic point of view; the inhibition is independant of the intracellular acetate or pyruvate concentration.

Temperature Measurements on Mice Irradiated with Very High X-Ray Intensities

A certain dependency of average survival time of mice from high X-ray intensities has been observed by various authors[1]. RAJEWSKY[2] reports on findings with high intensity irradiation that the animals died during the exposure or shortly afterwards; e.g., 50% of the mice were dead after 50 s exposure and the second half of the animals remained alive for 30 s after termination of the irradiation. The dose rate was approximately 190,000 r/min.

The lethal effect caused by such a high dose rate could be due to a different mechanism as it is usually the case at lower dose levels and dose rates. RAJEWSKY observed that the animals surviving such an experiment for a short time were apathetic but had increased breathing activity and ruffled fur. After a short time the animals become excited and go into cramp like conditions and die. This is different to the usual symptoms of low intensity and low dose reactions of animals.

The observations described above seem to indicate that the animals could have gone into a shock. Based on these reports, we have considered therefore the possibility of thermal shock to be the reason of the dramatic events taking place. To prove this assumption we used a thermocouple (constantan-copper) arrangement. The electrical signal created in the thermocouples was fed into a Liston-Becker d.c. braker amplifier, Model No. 14. The output signals were continuously recorded by an Esterline-Angus M. A. chart recorder.

Mice approximately 20 g of weight were used for our experiments. Two mice were tied each to a separate aluminum support in such manner that any movement of the body except the head was impossible. The thermocouples were inserted between the skin and muscle of one of the hind thighs of each animal and securely fastened with a small piece of tape. One animal served as the non-irradiated control. A Machlett AEC 50 Beryllium window tube operated at 43 KVp, 40 m A and without filtration served as source of radiation. Calibration of the X-ray output with a Grenz ray dosimeter (Physikalisch-Technische Werkstatt, Freiburg, Germany) gave an approximate dose rate of 6×10^5 r/min at 5 cm TSD taking air absorption into consideration. Measurements performed by ROGERS[3] show that X-rays of such low energy are almost entirely absorbed within a few millimeters of tissue (1% transmission at a depth of 3·1 mm Al). Therefore practically all primary radiant energy is absorbed by the body of the mouse. Figure 1 gives the calibration curves at different amplifier gains obtained with the help of precision thermometers. Theoretically 5×10^5 to 1×10^6 r/min should produce a temperature rise of several degrees in 1 min. According to the graphs the temperature increased approximately 0·3 to 0·7°C in 1 min.

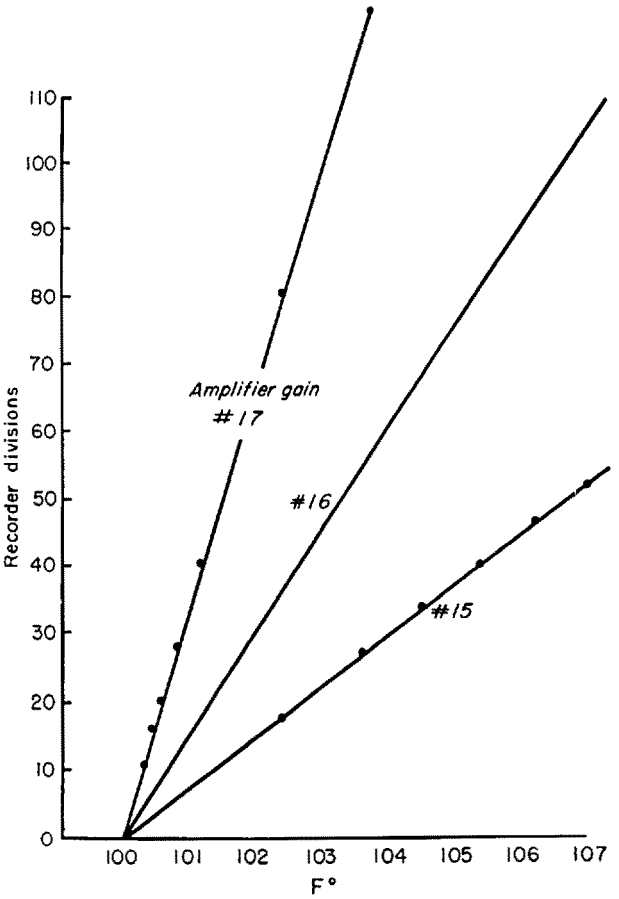


Fig. 1.

Figures 2 and 3, etc. show some examples of the temperature increase in the animals during X-ray exposure. Usually the temperature dropped again after irradiation was completed, except in two experiments where the temperature remained elevated for a longer period of

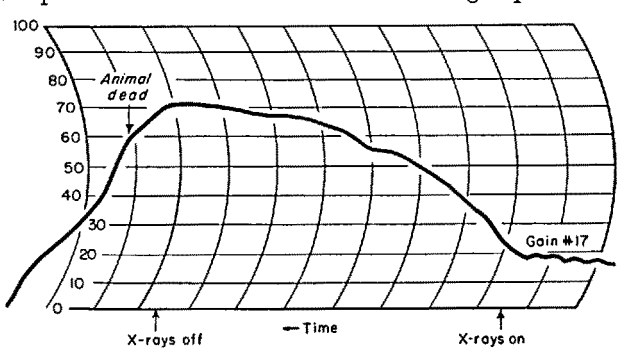


Fig. 2.

time. Also only in two cases animals died during the experiment after having received approximately 3×10^6 to 1×10^7 r. However all other animals died within 10 to 15 min after they were irradiated with 7×10^6 to 14×10^6 r.

[1] H. QUASTLER *et al.*, Amer. J. Physiol. *164*, 546 (1951). – E. P. CRONKITE, Radiology *56*, 661 (1951).

[2] B. RAJEWSKY *et al.*, Z. Naturforsch. *8*, 157 (1953).

[3] T. H. ROGERS, Radiology *48*, 594 (1947).

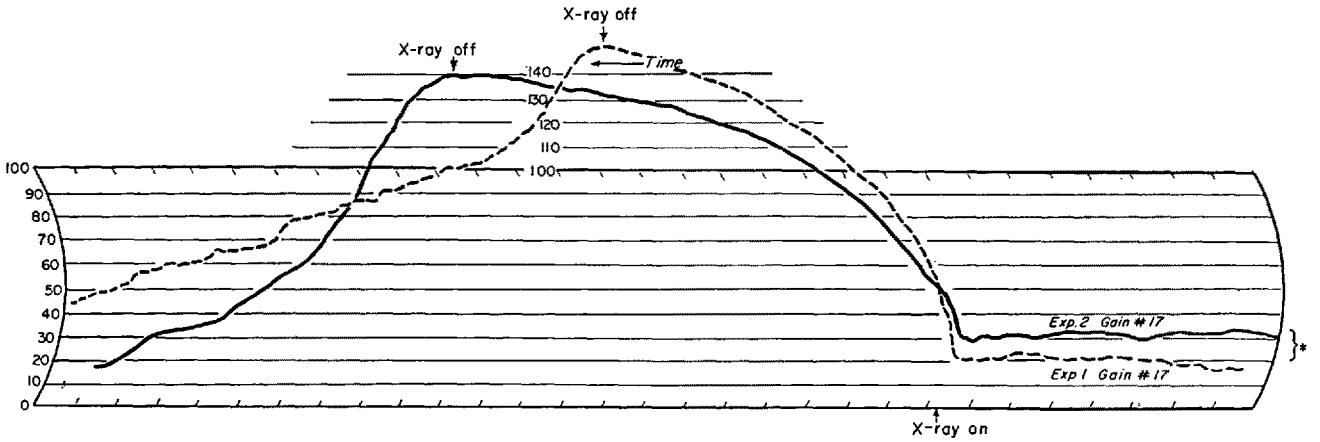


Fig. 3. * 0·3 cente degree

It is very well possible that the beam did not cover the animal uniformly at this target distance. However temperature increase of similar magnitude was also registered with the lower half of the mouse protected by lead. The beginning of such temperature changes was somewhat more delayed in this case.

Death could be noted almost immediately on the graph by a sharp temperature decrease. This was checked by killing one of two non-irradiated animals with a phenobarbital or air injection into the heart.

W. S. Moos

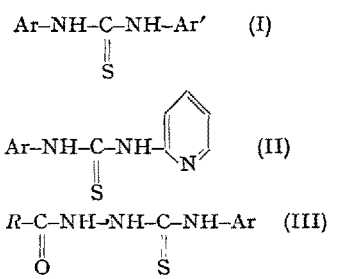
Department of Radiology, College of Medicine, University of Illinois, Chicago, August 18, 1955.

Zusammenfassung

Es wird untersucht, ob der nach sehr hohen Röntgendosen auftretende Letaleffekt bei weissen Mäusen durch einen thermischen Schock bedingt sein könnte. Subkutane thermoelektrische Temperaturregistrierung während der Bestrahlung mit $3{,}10^6$ bis 10^7 r (43 kV), (Berylliumfenster) ergab Temperaturanstiege von 1 bis 4° C während der Bestrahlung. Danach fällt die Temperatur meist wieder ab. Anzahl der Versuchstiere: 12.

Structure moléculaire et activité tuberculostatique dans le groupe des dérivés de la thiourée

L'activité importante contre les Mycobactéries de nombreux composés appartenant au groupe des N,N'-diarylthiourées a été établie par plusieurs travaux effectués au cours de ces trois dernières années[1]. Outre leur importance pratique, les substances de ce groupe, extrêmement nombreuses et faciles à synthétiser, constituent un matériel particulièrement commode pour l'étude des relations entre structure moléculaire et pouvoir tuberculostatique. Dans le présent travail, nous indiquons les activités tuberculostatiques *in vitro* pour une nouvelle série de plus d'une quarantaine de N,N'-diarylthiourées (I) et de N-aryl-N'-2-pyridylthiourées (II). L'activité a été déterminée sur *Mycobacterium tuberculosis* var. *hominis* (souche H 37 Rv), poussant sur milieu de Dubos au tween 80, et à la sérum-albumine; l'inoculat est constitué par une goutte d'une culture de 4 jours, et les lectures se font par comparaison avec des cultures témoins, après incubation à 37° pendant 1, 2 et 3 semaines.



Dans ces conditions, et en prenant les chiffres correspondants aux lectures faites après 14 jours d'incubation (ce choix a été fait afin de permettre la comparaison de nos résultats avec ceux obtenus par EISMAN, KONOPKA et MAYER, ces auteurs ayant adopté 14 jours comme durée d'incubation standard), nous avons obtenu les résultats suivants:

1° 12 des substances examinées ont montré une activité tuberculostatique importante à la concentration de 10^{-6} (1 γ par ml de culture). Ce sont les:

4-*n*-butoxy-4'-méthoxythiocarbanilide
4-*n*-butoxy-4'-*n*-propoxythiocarbanilide
4-*n*-butoxy-4'-isobutoxythiocarbanilide
4-isoamyloxy-4'-isobutoxythiocarbanilide
4-*n*-amyloxy-4'-hydroxythiocarbanilide
4-*n*-amyloxy-4'-diméthylaminothiocarbanilide
4-isobutoxy-2'-phénylthiocarbanilide
4-fluoro-2',5'-diméthoxythiocarbanilide
4-chloro-4'-fluorothiocarbanilide
N-*p*-éthoxyphényl-N'-α-naphtylthiourée
N,N'-di(α-naphtyl)thiourée
N-*p*-fluorophényl-N'-α-pyridylthiourée

Cette activité diminue en général fortement lorsqu'on passe aux lectures faites après 3 semaines d'incubation.

2° 10 des substances examinées ont montré une activité tuberculostatique importante à la concentration de 10^{-5} (10 γ par ml de culture). Ce sont les:

[1] R. L. MAYER, P. C. EISMAN et E. A. KONOPKA, Proc. Soc. exper. Biol. Med. *82*, 769 (1953). – C. F. HUEBNER, J. L. MARSH, R. H. MIZZONI, R. P. MULL, D. C. SCHROEDER, H. A. TROXELL et C. R. SCHOLZ, J. Amer. chem. Soc. *75*, 2274 (1953). – N. P. BUU-HOÏ et N. D. XUONG, C. r. Acad. Sci. Paris *237*, 498 (1953). – P. C. EISMAN, E. A. KONOPKA, R. L. MAYER *et al.*, Amer. Rev. Tuberc. *70*, 121, 130 (1954). – N. P. BUU-HOÏ, Int. J. Leprosy *22*, 16 (1954). – E. A. KONOPKA, T. GISI, P. C. EISMAN et R. L. MAYER, Proc. Soc. exper. Biol. Med. *89*, 388 (1955). – N. P. BUU-HOÏ, N. D. XUONG, N. H. NAM, J. M. GAZAVE, J. PILLOT et M^lle L. SCHEMBRI, Exper. *11*, 97 (1955). – N. P. BUU-HOÏ, N. B. KHUYEN et N. D. XUONG, Bull. Acad. méd. (Paris) *15/16*, 275 (1955). – N. P. BUU-HOÏ, N. D. XUONG et N. H. NAM, J. chem. Soc. *1955*, 1573.