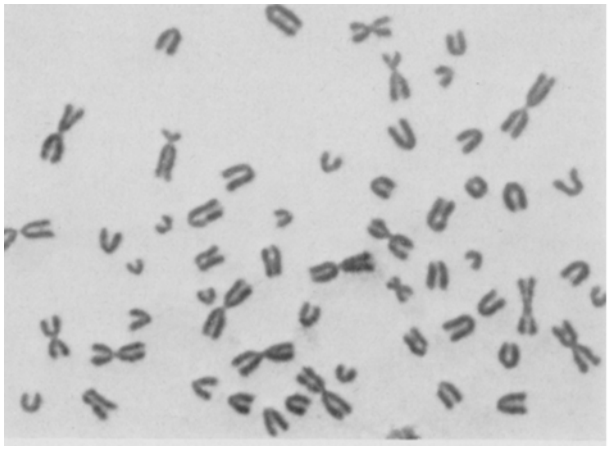

Fig. 2. L-cell with a total of 60 chromosomes and 17 non-acrocentric chromosomes.

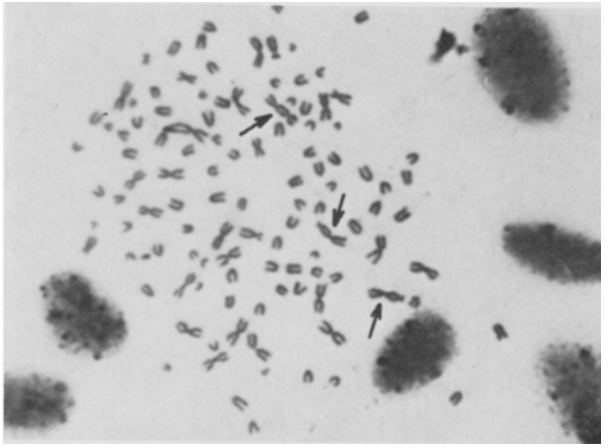

Fig. 3. Paratetraploid L-cell with dicentric chromosomes (arrows).

gentamicin, 500 µg/ml, followed by two passges with 100 µg/ml, did not induce obvious changes in the numerical characteristics of the L-cell chromosomes. When an initial treatment with 500 µg/ml gentamicin was followed by five passages with 100 µg/ml, the proportion of cells showing 60 chromosomes fell to less than 30% (Figure 1, b and c).

Duration of treatment with gentamicin also affected chromosome structure. Whereas only 4 chromatid gaps were observed in the controls, severe aberrations such as chromosome fragments and dicentrics were frequent in L-cells (Table) maintained during five passages in the presence of gentamicin 100 µg/ml (Figure 2). It should also be pointed out that such treatment decreased significantly the mitotic index. The effect of only two passages in the presence of gentamicin appeared to give an intermediate effect.

Several antibiotics such as mitomycin[8], streptonigrin[9], patulin[10], phleomycin[11] and daunomycin[12–14] have been reported to induce chromosome aberrations in cultured cells and especially in human leukocytes. Since, as shown in this paper, gentamicin has similar effects, it appears mandatory to control permanently the different characteristics of the cell strains used for experimental purposes.

Résumé. Les effets de la gentamicine ont été étudié sur des cellules de la lignée L. Une culture en présence de gentamicine à la dose de 500 µg/ml suivie de 5 passages à des concentrations de 100 µg/ml diminue jusqu'à 30% le nombre de cellules possédant 60 chromosomes et entraîne l'apparition d'anomalies chromosomiques telles que des fragments et des dicentriques. Lorsque la culture initiale est suivie de 2 passages seulement à 100 µg/ml on n'observe aucun changement numérique mais un taux intermédiaire d'anomalies de structure.

A. Léonard and S. Botis[15]

Radiobiology Department, C.E.N.-S.C.K., Boeretang 2000, B–2400 Mol (Belgium), 22 October 1974.

[8] M. W. Shaw and M. M. Cohen, Genetics *51*, 181 (1965).
[9] M. M. Cohen, M. W. Shaw and A. P. Craig, Proc. natn. Acad. Sci. USA *50*, 16 (1963).
[10] R. F. J. Withers, Symp. Mutational Process, Mech. Mutation Inducing Factors (Praha 1965), p. 359.
[11] N. F. Jacobs, R. L. Neu and L. I. Gardner, Mutation Res. *7*, 251 (1963).
[12] B. K. Vig, S. B. Kontras and A. M. Aubell, Mutation Res. *7*, 91 (1969).
[13] B. K. Vig, S. B. Kontras, E. F. Paddock and L. D. Samuel, Mutation Res. *5*, 279 (1968).
[14] B. K. Vig, S. B. Kontras and L. D. Samuel, Experientia *24*, 271 (1968).
[15] This work has been done with grants from the 'Fonds National de la Recherche Scientifique Medicale' and from the 'Caisse Générale d'Epargne et de Retraite'. We are grateful to Mr. F. Schepens and Mr. G. Decat for skilled technical assistance.

The Calorigenic Action of Norepinephrine in Rats After Hypophysectomy

Starting from distinct age-dependent effects of catecholamines on oxygen consumption in rats[1–4], it was supposed that growth hormone influences the calorigenic effects of sympathicomimetics.

Preceding investigations in rats revealed that 5 days after hypophysectomy the effect of norepinephrine on oxygen consumption was abolished, whereas the action of 2,4 DNP was hardly changed[5]. The question arose whether the intact hypophysis or only the presence of pituitary hormones are necessary for the calorigenic effects of norepinephrine.

Therefore investigations were carried out shortly after hypophysectomy, when pituitary hormones are still

[1] H. Ankermann, Acta biol. med. germ. *12*, 711 (1964).
[2] D. Müller and H. Ankermann, Acta biol. med. germ. *23*, 819 (1969).
[3] D. Müller and H. Ankermann, Acta biol. med. germ. *24*, 673 (1970).
[4] F. W. Tiller, D. Müller and H. Ankermann, Acta biol. med. germ. *27*, 619 (1971).
[5] H. Ankermann, F. W. Tiller, L. Kersten and D. Müller, Experientia *28*, 476 (1972).

present in the organism, and 7 days later. 22-day-old Wistar rats were hypophysectomized[6], and 2–4 h as well as 7 days after the operation norepinephrine (0.6 mg/kg) was administered i.p., and the oxygen consumption and CO_2 output were measured as previously described[4].

Norepinephrine enhances oxygen consumption of 22-day-old sham-operated control rats very strongly (Figure 1, A). In rats having been hypophysectomized 2–4 h before, the norepinephrine effect was as great as in control rats (Figure 1, A). 7 days later (29th day of life) norepinephrine enhances the oxygen consumption of control rats somewhat less than 1 week previously (Figure 1, B). This decrease of efficacy corresponds to the known age-dependent changes in the calorigenic action of catecholamines[2–4]. 7 days after hypophysectomy, norepinephrine failed to increase oxygen consumption (Figure 1, B), thus confirming former results[5]. Similar results were obtained when CO_2 output was measured (Figure 2).

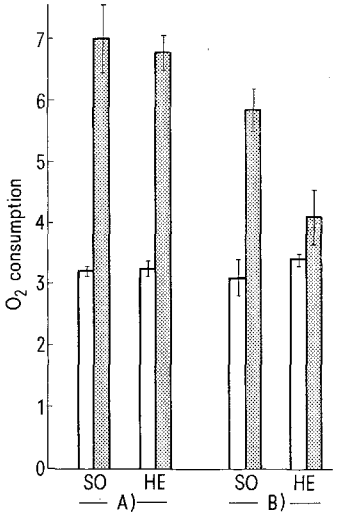

Fig. 1. Influence of norepinephrine (0.6 mg/kg body wt.) upon oxygen consumption (ml/min/100 g body wt. ± S.E.M.) in control (sham-operated) and hypophysectomized rats. A) 22-day-old rats 2–4 h after sham-operation (SO) or hypophysectomy (HE). B) 29-day-old rats 7 days after sham-operation (SO) or hypophysectomy (HE). □, Oxygen consumption before norepinephrine administration; ▨, oxygen consumption after norepinephrine administration.

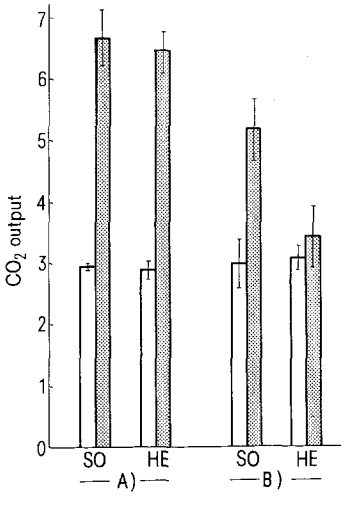

Fig. 2. Influence of norepinephrine (0.6 mg/kg body wt.) upon CO_2 output (ml/min/100 g body wt. ± S.E.M.) in control (sham-operated) and hypophysectomized rats. For further explanations cf. legend of Figure 1.

Obviously the hypophysis as an intact organ is not essential for the calorigenic action of catecholamines, as the results 2–4 h after hypophysectomy indicate. The failure of norepinephrine to enhance the oxygen consumption 7 days after hypophysectomy may be caused by the lack of pituitary hormones. Several possible secondary changes do not come in question. The secondary insufficiency of the adrenal cortex and the thyroid gland seems to be without importance because the calorigenic action of sympathicomimetics was abolished neither by adrenalectomy[7] nor by treatment of rats with methylthiouracil[8]. Likewise a possible nonspecific injury of the hypophysectomized rats cannot be responsible for the impairment of calorigenic actions because the enhancement of O_2 consumption due to 2,4-DNP was not changed under these conditions[5].

Considering the age dependence of the calorigenic action of catecholamines, it is supposed that among pituitary hormones the participation of growth hormone in metabolic responses to catecholamines may be important, particularly as the plasma level of growth hormone is higher in young rats than in adult ones[9]. Moreover, it is known that growth hormone is essential for other metabolic effects of norepinephrine, like lipolysis[10–12].

A further clarification of the role of pituitary hormones for calorigenic action of norepinephrine would be the substitution of these hormones after hypophysectomy.

Zusammenfassung. 2–4 h nach Hypophysektomie erhöht Noradrenalin den Sauerstoffverbrauch wie bei Kontrollratten, 7 Tage nach der Entfernung der Hypophyse ist jedoch diese Wirkung des Noradrenalin aufgehoben. Die CO_2-Abgabe verhält sich qualitativ wie der Sauerstoffverbrauch.

D. MÜLLER, L. KERSTEN and H. ANKERMANN

Institut für Pharmakologie und Toxikologie der Friedrich-Schiller-Universität Jena, Zentraler Platz, DDR-69 Jena (German Democratic Republic, DDR); and Akademie für ärztliche Fortbildung der Deutschen Demokratischen Republik, Berlin (DDR),
1 October 1974.

[6] F. E. D'AMOUR and R. R. BLOOD, *Manual for Laboratory Work in Mammalian Physiology* (University of Chicago Press, Chicago 1956).
[7] H. ANKERMANN, Acta biol. med. germ. *8*, 489 (1962).
[8] F. W. TILLER, D. MÜLLER and H. ANKERMANN, Arch. int. Pharmacodyn. Ther. *198*, 377 (1972).
[9] J. T. WILSON and L. A. FROHMAN, J. Pharmac. exp. Ther. *189*, 255 (1974).
[10] H. M. GOODMAN and E. KNOBIL, Proc. Soc. exp. Biol. Med. *115*, 849 (1964).
[11] H. M. GOODMAN, Proc. Soc. exp. Biol. Med. *132*, 821 (1969).
[12] H. M. GOODMAN, Endocrinology *86*, 1064 (1970).