The proportion of the different aberrations was analysed (Figures 1 and 2a and b).

In the above-mentioned experimental conditions, neither copper nor zinc increased the amount of damage in meiosis of the generation X1. However, the proportions of several kinds of aberrations were different for the three treatments.

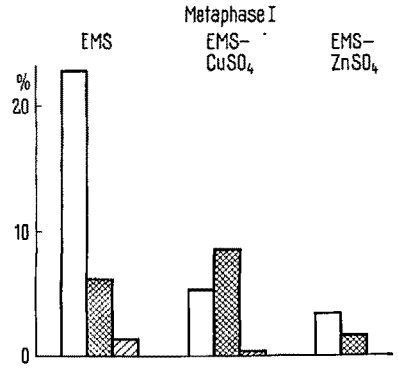

Fig. 1. Percentages of aberrations observed at metaphase I (±300 metaphases; EMS conc. 0.3 g/100 ml; $CuSO_4$ or $ZnSO_4$ conc. 0.03 mg/100 ml). White: ring of four (or six). Cross-ruled: figures of eight. Hatched: chains of four.

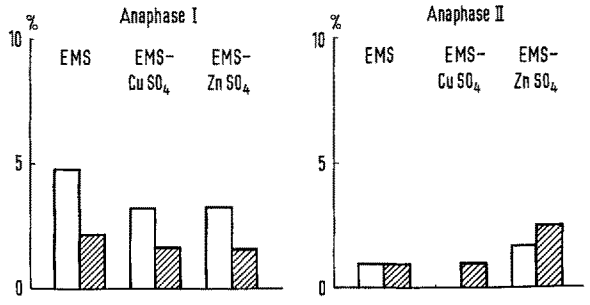

Fig. 2a and 2b. Percentages of aberrations observed at anaphases I and II (±300 anaphases). White: bridges. Hatched: fragments.

The frequency of rings of four was higher without copper or zinc, but the proportion of figures of eight was higher with EMS-copper treatment (Figure 1). In this last case, the figures of eight were found to be more frequently asymmetrical although correctly coorientated at the equatorial plate.

This indicates that chromosome translocations should differ qualitatively from those appearing after the other treatments.

The different proportions of aberrations are not so evident for anaphases, these aberrations being in fact much less specific than in metaphase.

Comparing Figures 1 and 2a and b, it can also be seen that for all treatments, the number of aberrations decreases from metaphase I to anaphase II.

At anaphase I, the percentage of bridges (both chromatid and chromosome) is significantly higher than the percentage of fragments (Figure 2a), whereas this situation is almost reversed for anaphase II (Figure 2b).

The data presented here show that EMS treatments of barley seeds result in meiotic aberrations which will influence the mutation spectrum of the generation X2.

They also show that salts could also be used for changing the relative proportions of these chromosome aberrations[7].

Résumé. Des semences sèches d'orge ont été traitées respectivement par des solutions d'EMS et d'EMS additionnées de sulfate de cuivre ou de sulfate de zinc. Nous avons montré qu'il en résulte des aberrations chromosomiques en méïose au cours de la génération traitée (X1). L'adjonction aux solutions de l'un ou de l'autre sel n'a pas accru la quantité de lésions observées, mais a fortement modifié la proportion des différents types d'aberrations chromosomiques.

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[7] Work subsidized by the Centre National d'Etude des Mutations (Belgique).

Effect of α-Methyldopa and α-Methyl-*m*-tyrosine on the Mobilization of Free Fatty Acids

It has been well established that the sympathetic nervous system plays an important role in the mobilization of free fatty acids (FFA) from adipose tissue. The sympathetic transmitter substance norepinephrine has frequently been shown to mobilize FFA *in vivo* and *in vitro*[1], presumably by stimulating a lipolytic system in adipose tissue[2]. Since adipose tissue contains considerable amounts of norepinephrine[3-5] and enzymes connected with its synthesis and metabolism[5], it is safe to assume that norepinephrine also serves as sympathetic transmitter in adipose tissue.

Recently we were able to demonstrate that the injection of tyramine and other aromatic monoamines which act through the release of norepinephrine from storage sites in sympathetic nerve endings[6] also produces mobilization of FFA from adipose tissue triglycerides, as indicated by the elevated plasma levels of FFA and glycerol[7]. This effect of tyramine was absent if the adipose tissue norepinephrine had previously been depleted by reserpine[7].

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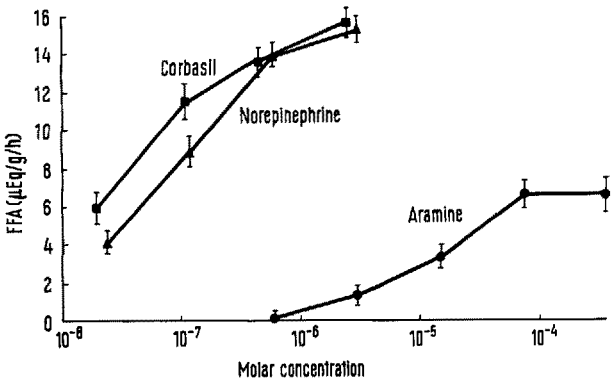
Effect of syrosingopine, α-methyl-Dopa and α-methyl-*m*-tyrosine on the free fatty acid mobilization by tyramine
Male Wistar rats (160–180 g) were kept on standard pellet diet *ad libitum* until the experiments. Pretreatment: 0.3 mg/kg syrosingopine (Su 3118) were injected s.c. 15 and 20 h prior to the experiment; 200 mg/kg l-α-methyl-dopa (α-MD) and dl-α-methyl-*m*-tyrosine (α-MMT) were given s.c. daily for 1–3 days, the last injection 15 h before the experiment. 15 min after the injection of tyramine (10 mg/kg s.c.) the animals were killed for the determination of plasma free fatty acids (FFA) according to the method of DOLE[13] and expressed as μEq/ml plasma ± standard error of the mean (s.e.). *n* = Number of animals.

Experiment No.	Group	Dosage mg/kg	*n*	FFA (μEq/ml plasma ± s.e.) –	+Tyramine	*P* value
1	Controls	–	25	0.217 ± 0.010	0.599 ± 0.017	<0.001
2	Su 3118	2 × 0.3	10	0.230 ± 0.024	0.247 ± 0.017	>0.50
3	α-MD	1 × 200	5	0.180 ± 0.033	0.575 ± 0.074	<0.005
	α-MD	3 × 200	5	0.215 ± 0.050	0.415 ± 0.045	<0.005
4	α-MMT	1 × 200	5	0.213 ± 0.032	0.282 ± 0.015	>0.10
	α-MMT	3 × 200	5	0.225 ± 0.022	0.230 ± 0.015	>0.80

α-Methyldopa (α-MD) and α-methyl-*m*-tyrosine (α-MMT) also cause depletion of tissue norepinephrine[8]. This effect, however, differs from that of reserpine in that norepinephrine is not only depleted but also replaced by α-methylnorepinephrine (Corbasil) and metaraminol (Aramine), the metabolic products of α-MD and α-MMT respectively[9–12], which then may serve as 'false transmitters'[9,11].

Following the subcutaneous injection of 10 mg/kg of tyramine, the plasma FFA level of rats rose by nearly 200% within 15 min (Table, Experiment No. 1). Pretreatment with the reserpine analogue syrosingopine (Su 3118), which lowered the norepinephrine content of adipose tissue by 85%, completely prevented the tyramine-induced rise in plasma FFA (Table, Experiment No. 2).

Pretreatment with *l*-α-MD also led to a substantial reduction of the norepinephrine content in adipose tissue to about 25% of the control values. The FFA mobilizing effect of tyramine, however, was essentially unchanged or somewhat reduced only after 200 mg/kg of *l*-α-MD had been given on three consecutive days (Table, Experiment No. 3). Different results were obtained with α-MMT; although this amino acid reduced the adipose tissue norepinephrine content at least to the same degree as α-MD, FFA mobilization by tyramine was strongly inhibited already after a single injection of 200 mg/kg of α-MMT, and 3 × 200 mg/kg of α-MMT completely blocked the action of tyramine (Table, Experiment No. 4).



Lipolytic activity of norepinephrine, corbasil (α-methyl-norepinephrine) and aramine (metaraminol) *in vitro*. Pieces of epididymal fat pads (60–100 mg) of fed rats (160–180 g) were incubated essentially following the method of JUNGAS and BALL[15] for 60 min at 37°C with varying concentrations of the amines in albumin-free Krebs-Ringer phosphate buffer pH 7.2. The accumulation of free fatty acids in the adipose tissue was determined according to the method of DOLE[13], corrected for spontaneous lipolytic activity and expressed as μEq/g tissue/h ± standard error of the mean (s.e.). Each point represents the average of 3–6 experiments.

Experiments *in vitro* were performed in which the lipolytic activities of α-methylnorepinephrine (Corbasil) and metaraminol (Aramine) were determined and compared with that of norepinephrine. Norepinephrine and corbasil were about equally effective in promoting the accumulation of FFA in pieces of epididymal fat of rats incubated in albumin-free Krebs-Ringer phosphate buffer which agrees with preliminary results obtained in the hamster by RUDMAN et al.[14]. As can be seen from the Figure the maximal net accumulation of about 15.0 μEq/g tissue/h was observed if both compounds were present at a molar concentration of $3 \cdot 10^{-6}$, while half-maximal values were obtained at a concentration of $3\text{–}6 \cdot 10^{-7} M$. Aramine, however, proved to be at least a thousand times less active than norepinephrine and corbasil. Its dose-response curve not only differed in slope from those of the other compounds, but never exceeded a maximal value of 6.0 μEq/g/h at concentrations above $10^{-4} M$.

If it is assumed that in adipose tissue also the major part of the natural sympathetic transmitter norepinephrine is replaced by corbasil or aramine after pretreatment with α-MD or α-MMT, the conclusion seems justified that corbasil, in contrast to aramine, serves as a 'false' but rather efficient transmitter in mediating the FFA mobilizing effect of tyramine.

Zusammenfassung. Die fettsäurenmobilisierende Wirkung des Tyramins an Ratten liess sich durch Vorbehandlung mit α-Methyl-*m*-Tyrosin, nicht jedoch mit α-Methyl-Dopa verhindern. *In vitro* war die lipolytische Wirkung des aus α-Methyl-Dopa entstehenden α-Methyl-Noradrenalin (Corbasil) mehr als 1000mal stärker als diejenige des aus α-Methyl-*m*-Tyrosin entstehenden Metaraminol (Aramin).

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Pharmakologisches Institut der Universität Frankfurt/Main (Western Germany), March 18, 1964.

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