kind of mosaicism has indeed been observed after treatment with X-rays[2,3] and mustard gas[4]; in other cases the deficiency may not have been accessible to analysis, or it may not have given rise to viable tissue.

The origin of such a duplication-deficiency in the newly fertilized zygote need not involve a true delayed effect, but only differences in the way in which the broken sister chromatids undergo reunion. X-ray duplications presumably arise by this mechanism. Their frequency in Bauer's experiments[5] was seven duplications out of 688 structural changes; Kaufmann[6] found a similar frequency. After mustard gas treatment of males, Mehtab[7] obtained two reversed repeats among eleven structural changes. Added to the present sample, this gives a frequency of three reversed repeats among twenty-seven changes, a markedly higher value than that found for X-rays. It suggests that some special effect of chemical treatment, probably its after-effect, favours the occurrence of repeats. It should also be noted that reverse repeats cannot arise without previous breakage of the chromosomes; the frequent occurrence of this type of change after mustard gas treatment indicates that at least many of the structural changes induced by mustard gas cannot be explained by non-homologous crossing-over (see ref. 8).

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## Inability of Acetylcholine Antagonists to protect Mice against the Toxicity of 'Tensilon'

THE anticurare action of 'Tensilon' (3-hydroxy-*N*-dimethylethylanilinium bromide) was considered by Randall[1,2] not to depend upon cholinesterase inhibition. Hobbiger[3] and Hall and Parkes[4] showed, however, that 'Tensilon' does not reverse neuromuscular block after treatment of the preparation with tetraethyl pyrophosphate, implying the necessity of active cholinesterase for the effect.

We have recently described the protection afforded to mice against the toxicity of anticholinesterase drugs by antagonists of acetylcholine[5]. Animals were injected intravenously with atropine, 10 mgm./kgm., tubocurarine, 0·1 mgm./kgm., or hexamethonium, 40 mgm./kgm., and the decrease in intravenous toxicity of simultaneously injected neostigmine or tetraethyl pyrophosphate may be quoted as examples:

| | Neostigmine | Tetraethyl pyrophosphate |
|---|---|---|
| *LD* 50 alone | 0·306 mgm./kgm. | 0·2 mgm./kgm. |
| *LD* 50 with atropine | 0·66 ,, | 0·56 ,, |
| *LD* 50 with tubocurarine | 4·19 ,, | 0·73 ,, |
| *LD* 50 with hexamethonium | 4·5 ,, | 0·666 ,, |

Corresponding values obtained with 'Tensilon' have shown, however, that these antagonists provided no protection at all against the toxicity of this substance.

| | |
|---|---|
| *LD* 50 of 'Tensilon' alone | 18·6 (17·6–19·6) mgm./kgm. |
| *LD* 50 with atropine | 17·4 (16·35–18·5) ,, |
| *LD* 50 with tubocurarine | *c.* 20 mgm./kgm. (2 dose-levels only) |
| *LD* 50 with hexamethonium | 17·6 (16·45–18·8) mgm./kgm. |

These results would certainly seem to be inconsistent with the participation of cholinesterase inhibition or the augmentation of cholinergic function in the toxicity of 'Tensilon'.

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## Toxicity of Erythromycin

IN the course of experiments using young guinea pigs as test animals, it was found that erythromycin given orally or intraperitoneally caused the animals to look ill after two to three days, with ruffled fur, anorexia, disinclination to move and subnormal temperature, followed by death on the sixth to eighth day with emaciation and signs of diarrhœa. No obvious common cause of death could be found macroscopically or microscopically in sections of liver, spleen, kidney or lung, although occasionally liver necrosis and renal tubular degeneration were seen, accompanied by albuminuria, red cells and casts in the urine and slightly raised blood urea.

It may be seen from Table 1 that, with small numbers of animals, toxicity is independent of age (weight) of the animal or the type of preparation, but is related to the dosage and route of administration, that is, blood and tissue concentration. Guinea pigs weighing 160 gm. were given erythromycin orally or intraperitoneally in doses of 62·5 mgm./kgm. at 12-hr. intervals, and killed 2 hr. after the third dose. The serum and liver concentrations were 2 μgm./ml. and 16 μgm./ml. respectively after injection, and 0·1–0·2 μgm./ml. and 0·9 μgm./ml. orally. A high degree of toxicity is indicated by the lethality of 500–600 μgm./kgm. injected in one dose, where the blood and tissue concentrations must have been extremely low and transient. Guinea pigs injected intraperitoneally with 100 mgm. erythromycin (625 mgm./kgm.) died in 3–6 hr. Doses used as in Table 1 caused death in 3–12 days, averaging 7·1 ± 0·2 days for forty-five guinea pigs.

Hamsters of 50–60 gm. weight treated intraperitoneally with 30–200 mgm./kgm. erythromycin in one or more doses also died after approximately thirteen days, with a terminal illness closely resembling that of guinea pigs.

This delayed toxicity has not been recorded in other work on erythromycin, where the oral *LD*50