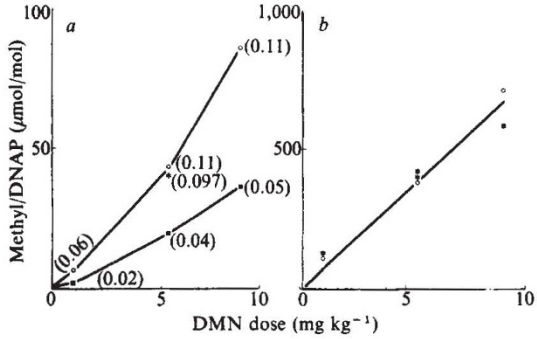

Fig. 2 Amounts of O^6-methylguanine (*a*) and 7-methylguanine (*b*) in the liver DNA of control (○) and AAF-pretreated (■) rats 5 h after administration of (^{14}C-methyl)-labelled DMN at 1, 5.5 and 9 mg kg^{-1} (specific activity 11 mCi mmol^{-1} for lowest dose and 5 mCi mmol^{-1} for higher two doses). Liver DNA was prepared and analysed as previously described (see Table 1 legend) and the 5 h values are taken from lines of best fit for results obtained for animals killed over a 48 h period. Lines of best fit were derived as follows: *a*, quadratic curves ($P < 0.05$ in each case) for AAF-pretreated rats; Gompertz curves were fitted for the control data; *b*, least square regression lines (coefficient of multiple correlation $R > 0.98$ in each case). The ratios of the amounts of O^6-methylguanine to 7-methylguanine are given in parentheses adjacent to the appropriate points. Values of these methyl purines taken from Table 1.

occurs to such an extent that there is no detectable inhibition of the repair process at all (Fig. 3*b*). Some recent reports have shown that chronic treatment with agents which produce O^6-methylguanine in DNA can also induce the repair of these lesions. This has been observed for rat liver DNA following chronic administration of DMN[9], in several organs of the rat following repeated injections of dimethylphenyltriazene[10] and for *Escherichia coli* following pretreatment with *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine[11].

In the AAF-pretreated animals the reason for the observed increase in the ratio of methylpurines at around 8 h (Fig. 3*b*) is obscure, but as metabolism of DMN is complete by the fifth hour no further increase in the amount of alkylation at the O^6-position of guanine could occur. Further, as reincorporation of this product is extremely unlikely[12], one possible explanation might be the induction of a specifically enhanced loss of 7-methylguanine over this short period: such a process has not yet been observed for rat liver DNA but this could be a side effect of the stimulation of the system for the repair of O^6-methylguanine in AAF-pretreated rats. For comparison, evidence for the repair

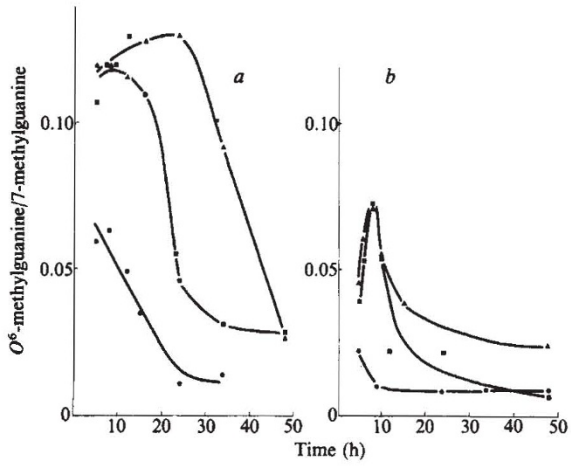

Fig. 3 Ratio of O^6-methyl- to 7-methylguanine in liver DNA in control (*a*) and AAF-penetrated (*b*) rats at various times after injection (i.p.) of (^{14}C-methyl) labelled DMN at 9 mg kg^{-1} (▲), 5.5 mg kg^{-1} (■) and 1 mg kg^{-1} (●).

of 7-methylguanine has been given in certain cases, for example in the DNA of the livers of mice[13] and of Syrian hamsters[14].

In conclusion, we have observed a dose-related repair of O^6-methylguanine in normal rats which, in agreement with previous work[6,15], is relatively more active at lower doses of DMN. Furthermore, a similar repair process is also present in AAF-pretreated rats, but here the repair of O^6-methylguanine is significantly enhanced at all doses used (Fig. 3). This effect is particularly evident at early times and when compared to controls there is a two- to threefold decrease in the ratio of these methylated guanines. It is interesting that a prolonged exposure to one carcinogen can induce the repair of lesions formed in DNA by another chemically unrelated carcinogen. Such an effect might be due to the induction of a general repair mechanism, possibly analogous to the induction of post-replication repair observed in AAF-treated Chinese hamster cells[16]. Alternatively, this might also be explained by the activation of a more specific repair system due to the formation of small amounts of an AAF-adduct at the O^6-position of guanine in DNA, particularly as such lesions have now been reported for the reaction of another aromatic amine, 1-naphthylamine, with DNA[17]. The formation of a lesion at a common site and its subsequent control by similar or closely related repair systems, which is implicit in the latter interpretation, may be especially relevant to the concept of mechanisms of carcinogenesis arising from agents belonging to different classes of chemical carcinogens.

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1. Doll, R. *Nature* **265**, 589–596 (1977).
2. *W.H.O. Environmental Health Criteria* No. 5 (1978).
3. Loveless, A. *Nature* **223**, 206–207 (1969).
4. O'Connor, P. J., Saffhill, R. & Margison, G. P. in *Environmental Carcinogens* (eds Emmelot, P. & Kriek, E.) (Elsevier, Amsterdam, in the press).
5. Margison, G. P. & O'Connor, P. J. in *Chemical Carcinogens and DNA* (ed. Grover, P. L.) (CRC Press, West Palm Beach, in the press).
6. Pegg, A. E. & Hui, G. *Biochem. J.* **173**, 739–748 (1978).
7. Becker, F. F. *Cancer Res.* **35**, 1734–1736 (1975).
8. Heath, D. F. *Biochem. J.* **85**, 72–81 (1962).
9. Montesano, R., Bresil, H. & Margison, G. P. *Cancer Res.* **39**, 1798–1802 (1979).
10. Cooper, H. K., Hauenstein, E., Kolar, G. F. & Kleihues, P. *Acta neuropath. (Berl.)* **43**, 105–109 (1978).
11. Schendel, P. F. & Robins, P. E. *Proc. natn. Acad. Sci. U.S.A.* **75**, 6017–6020 (1978).
12. O'Connor, P. J. & Saffhill, R. *Chemico-Biol. Interact.* **26**, 91–102 (1979).
13. Nemoto, N. & Takayama, S. *Biochem. biophys. Res. Commun.* **58**, 242–249 (1974).
14. Margison, G. P., Margison, J. M. & Montesano, R. *Biochem. J.* **157**, 627–634 (1976).
15. Pegg, A. E. *J. natn. Cancer Inst.* **58**, 681–687 (1977).
16. D'Ambrosia, S. M. & Setlow, R. B. *Proc. natn. Acad. Sci. U.S.A.* **73**, 2396–2400 (1976).
17. Kadlubar, F. F., Miller, J. A. & Miller, E. C. *Cancer Res.* **38**, 3628–3638 (1978).
18. Kirby, K. S. & Cook, E. A. *Biochem. J.* **104**, 254–257 (1967).
19. Lawley, P. D. & Shah, S. A. *Biochem. J.* **128**, 117–132 (1972).

Corrigendum

In the letter 'Use of Panamanian sea urchins to test the molecular clock' by H. A. Lessios, *Nature* **280**, 599–601, line 4 in paragraph 6 should read '. . . in *Diameda* were 20 times higher than in *Echinometra*, we would . . .'

Erratum

In the letter 'Induction of sporulation in *Bacillus brevis* by peptide antibiotics' by H. Ristow *et al.*, *Nature* **280**, 165–166, in paragraph 2 line 6, for ". . . that of gramicidin D between t_1 and t_5.", read ". . . that of gramicidin D between t_1 and $t_{1.5}$." Also for the abscissa on the top of Fig. 1 "$t_1 \ldots t_7$", read "$t_0, t_1 \ldots t_6$".