matters arising

Membrane initiation of DNA synthesis

HOBART *et al.*[1] reported convincing autoradiographic evidence that DNA replication is initiated near or on the nuclear membrane in sea urchins. In their discussion of the difference between their results and those reported by others for mammalian cells[2–4], they raise the possibility that the latter results might arise from repair synthesis because, "... autoradiographic analysis cannot distinguish between replication and repair synthesis of DNA . . ." and "Such a situation would confuse the interpretation of autoradiographs in determining subnuclear sites of replication".

It is only remotely possible that this explanation is correct. DNA repair synthesis in undamaged mammalian cells is not detectable by even very sensitive methods[5], let alone autoradiography. In cells whose DNA molecules are severely damaged, repair synthesis (excision) never exceeds about 1% of the amount of semiconservative synthesis that would occur simultaneously in undamaged cells[6,7]; even this amount of repair synthesis would not be detectable by the electron microscope autoradiographic method used by Hobart *et al.*[1].

Thus, the explanation for the results showing a difference between sites of initiation of DNA synthesis in sea urchins[1] and in mammalian cells[2–4] is very likely other than the one proposed by Hobart *et al.*[1].

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HOBART *et al.* REPLY: We agree with Painter and Cleaver that it seems only remotely possible that repair synthesis of DNA could account completely for the differences between our results with sea urchins and those of others using mammalian cells. But, it remains to be determined if repair synthesis is indeed a minor activity in cells which have been maintained for prolonged periods of time in tissue culture and have been treated with various metabolic inhibitors to achieve synchronisation. In any case the results with sea urchin embryos, which are normally synchronous and in which semiconservative replication is undoubtedly the principle activity, indicate that DNA synthesis occurs on or near the nuclear membrane.

Pentobarbitone enhancement of the inhibitory action of GABA

BOWERY and Dray[1] have suggested that pentobarbitone reverses the effects of the γ-aminobutyric acid (GABA) antagonist bicuculline methochloride (BMC), on both the superfused rat superior cervical ganglion and rat medullary neurones *in vivo*, without potentiating the action of GABA on these tissues in the absence of BMC. Such an action does not readily account for the accentuation by pentobarbitone of inhibitions mediated by GABA in the mammalian central nervous system[2], except by antagonism of an as yet undetected endogenous GABA antagonist.

We have investigated the action of pentobarbitone on 31 dorsal horn interneurones and three Renshaw cells of eight low spinal cats anaesthetised i.p with either α-chloralose and urethane (40 and 400–800 mg per kg), diallyl barbituric acid and urethane (60 and 600 mg per kg) or pentobarbitone sodium (35 mg per kg). Amino acids, acetylcholine, and pentobarbitone were administered electrophoretically from solutions in the outer barrels of seven-barrel micropipettes, the 3.6 M NaCl-containing centre barrels of which were used to record extracellular action potentials of single neurones. The following solutions were

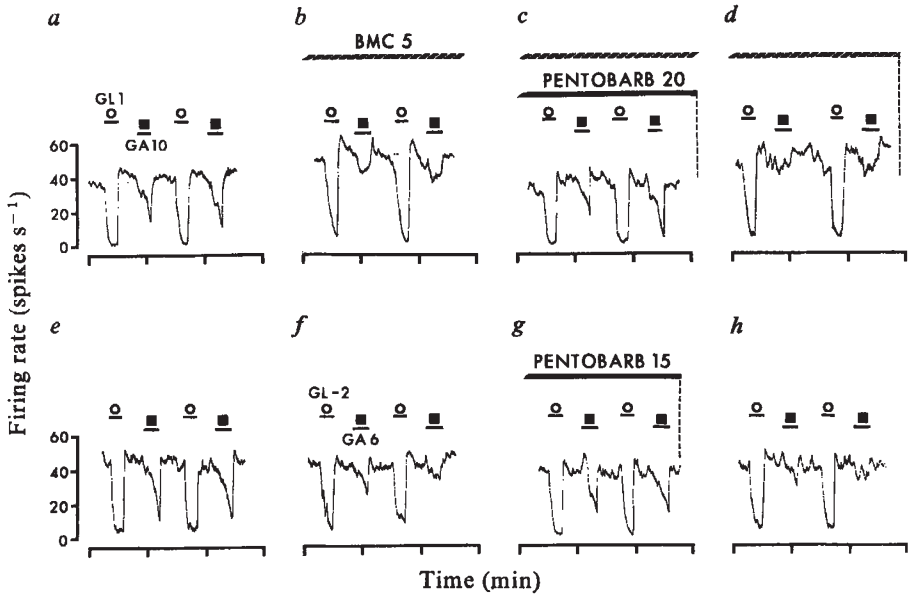

Fig. 1 Ratemeter records of the firing of a dorsal horn interneurone in a cat anaesthetised with α-chloralose and urethane. The electrophoretic ejection of glycine (GL) and GABA (GA) are indicated by the appropriate symbols, horizontal black lines and currents (nA). *b* and *c* were recorded 5 and 10 min after the commencement of the ejection of BMC which continued for 15 min, ceasing after *d*, as indicated by the broken vertical line. The ejection of pentobarbitone (PENTOBARB) commenced 3 min before *c* and again 2 min before *g*, and was also terminated at the vertical broken lines. Records *e* and *h* were 1 min after *d* and *g* respectively. Ordinates, firing rate, spikes s^{-1}, abscissae, time in min.